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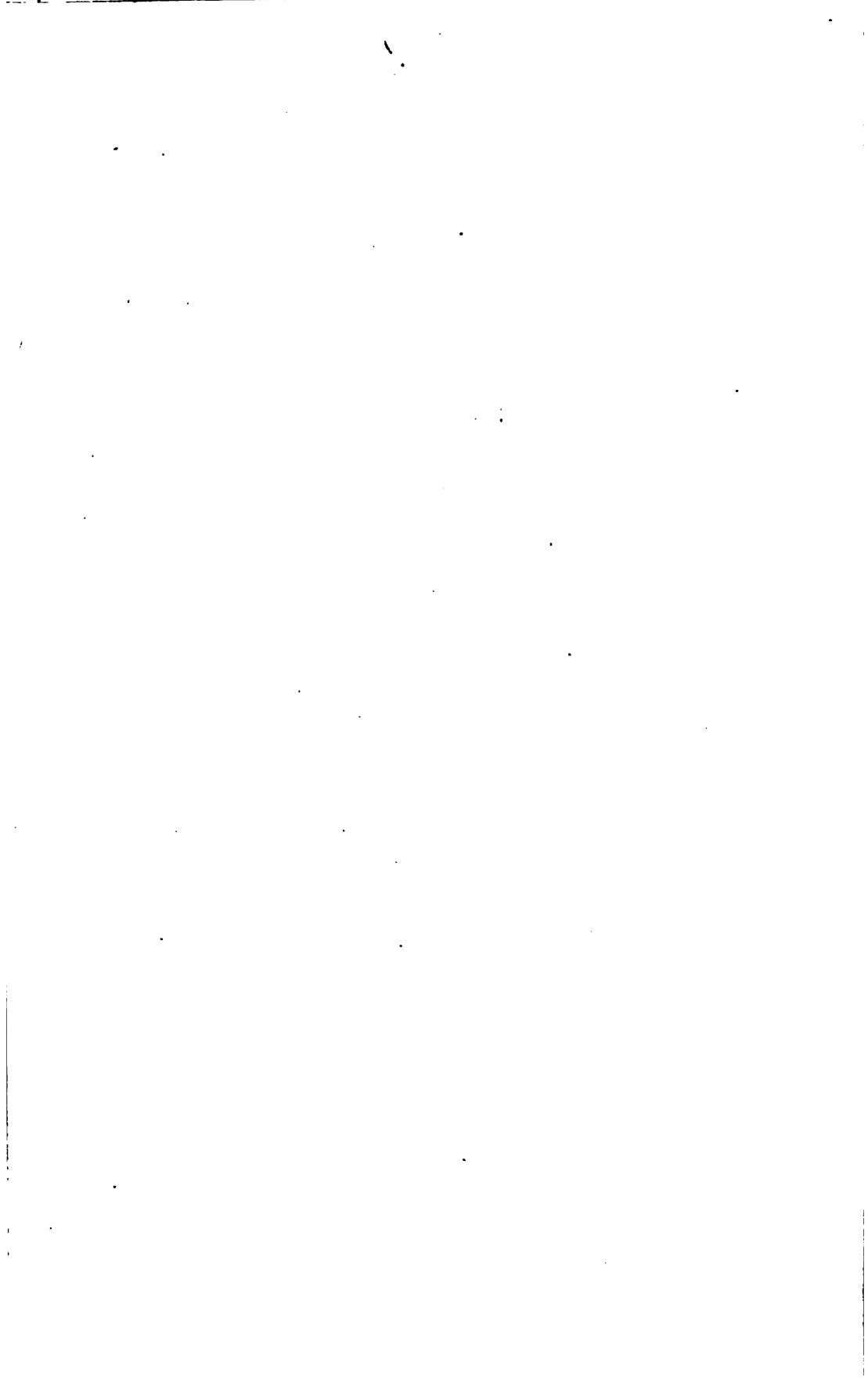
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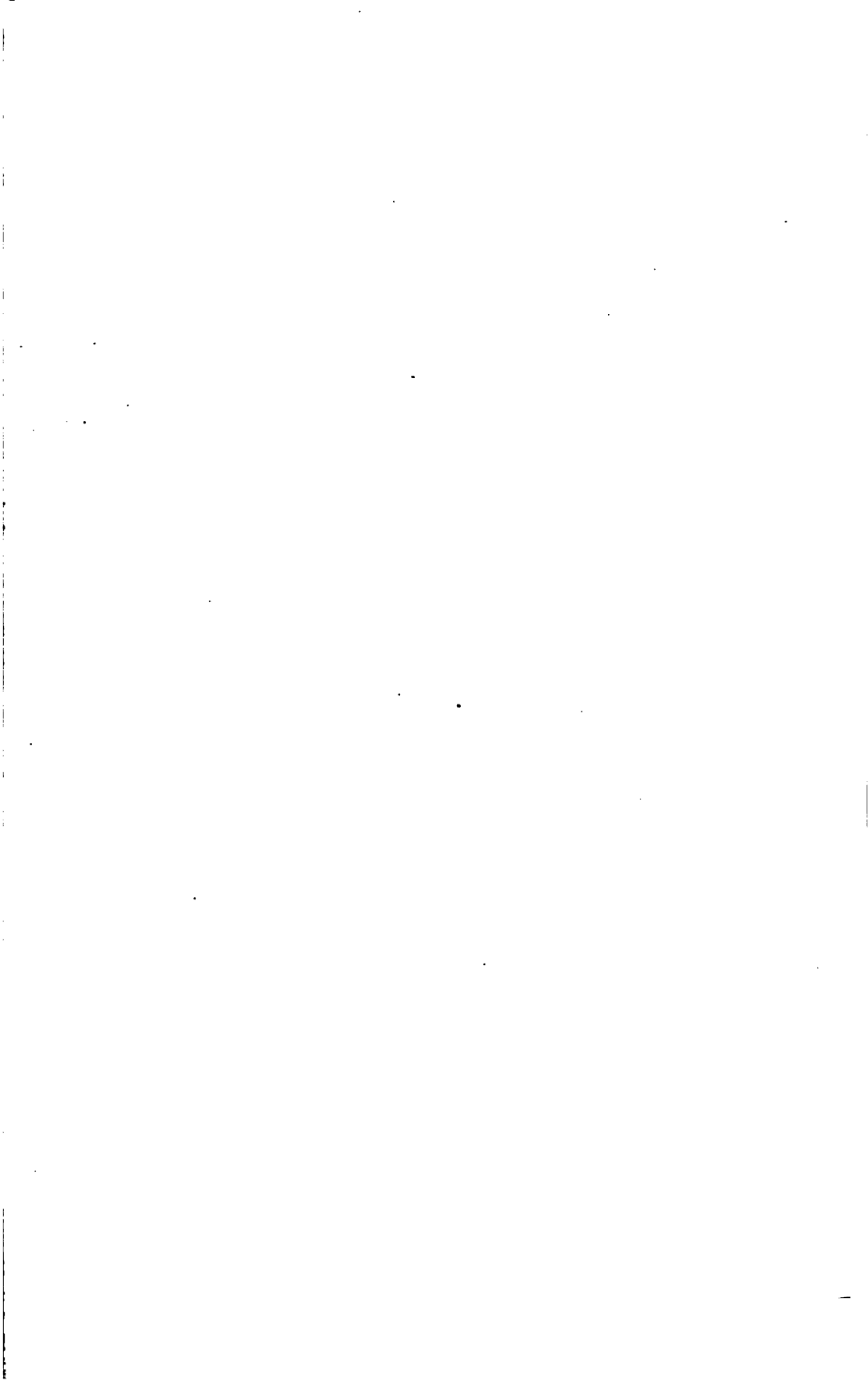
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*Awarded Grand Prize, Paris Exposition, 1900.*

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# PROGRESSIVE MEDICINE.

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES,  
AND IMPROVEMENTS

IN THE

MEDICAL AND SURGICAL SCIENCES.

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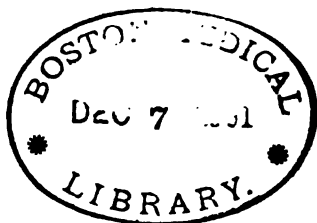
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VOLUME IV. DECEMBER, 1900.

DISEASES OF DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS,  
AND PERITONEUM—GENITO-URINARY DISEASES AND SYPHILIS—  
FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE  
EXTREMITIES, AND ORTHOPEDICS—DISEASES OF THE  
KIDNEYS—PHYSIOLOGY—HYGIENE—PRACTICAL  
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LEA BROTHERS & CO.,  
PHILADELPHIA AND NEW YORK.  
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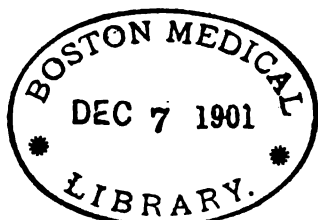


## CONTENTS OF VOLUME IV.

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|                                                                                                     | PAGE |
|-----------------------------------------------------------------------------------------------------|------|
| DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS,<br>THE LIVER, PANCREAS, AND PERITONEUM . . . . . | 17   |
| By MAX EINHORN, M.D.                                                                                |      |
| GENITO-URINARY DISEASES AND SYPHILIS . . . . .                                                      | 67   |
| By WILLIAM T. BELFIELD, M.D.                                                                        |      |
| FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE<br>EXTREMITIES, AND ORTHOPEDICS . . . . .      | 91   |
| By JOSEPH C. BLOODGOOD, M.D.                                                                        |      |
| DISEASES OF THE KIDNEYS . . . . .                                                                   | 223  |
| By JOHN ROSE BRADFORD, M.D., F.R.C.P.                                                               |      |
| PHYSIOLOGY . . . . .                                                                                | 277  |
| By ALBERT P. BRUBAKER, M.D.                                                                         |      |
| HYGIENE . . . . .                                                                                   | 303  |
| By HENRY B. BAKER, M.D.                                                                             |      |
| PRACTICAL THERAPEUTIC REFERENDUM . . . . .                                                          | 323  |
| By E. Q. THORNTON, M.D.                                                                             |      |
| INDEX . . . . .                                                                                     | 423  |





# PROGRESSIVE MEDICINE.

DECEMBER, 1900.

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## DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS, AND PERITONEUM.

By MAX EINHORN, M.D.

### THE ŒSOPHAGUS.

**Diverticulum of the Œsophagus.** Schwalbe<sup>1</sup> describes a case of traction diverticulum of the Œsophagus situated at its beginning, and corresponding to the cricoid cartilage. This is the usual seat of a diverticulum. The patient was forty-seven years of age, and complained of dysphagia of a more or less high degree for the last eleven years. The diagnosis was made from the following facts: A bougie always met with a resistance, which could not be overcome, at a distance of about 22 cm. from the teeth; a Mercier catheter could, after persistent manipulation, be introduced from the left side of the mouth into the Œsophagus and ultimately into the stomach; and a Röntgen photograph, after the patient had ingested a bismuth mixture, showed a shady area to the right of the manubrium sterni.

With regard to the etiology there is a dissension of opinion. Some writers assume a congenital defect, others a trauma as the starting-point for the diverticulum. The radical treatment consists in excision of the sac. This, however, is only done in extreme cases. In Schwalbe's patient the operation did not appear indicated, as he was able to partake of sufficient nourishment.

Yung<sup>2</sup> describes one case of a diverticulum situated low down in the Œsophagus, and one case of dilatation of the Œsophagus in consequence

<sup>1</sup> Ueber ein Pulsionsdivertikel. Münch. med. Wochenschr., 1899, No. 44.

<sup>2</sup> Zur Diagnose der Divertikel im unteren Abschnitt der Speiseröhre. Arch. f. Verdauungskrankh., 1900, Bd. vi., p. 45.

of spasmodic contraction of the cardia. Following the example of Rumpel, Yung used two tubes, one (provided with many side openings) leading into the gastric cavity and another (with one or two lower openings) into the œsophagus, in order to determine the existence of two cavities and also whether there was a diverticulum or not. He suggests, however, inserting within the stomach-tube another thin one with one opening at the bottom, serving the purpose of aspirating gastric contents through it.

**Spasm and Atony of the Œsophagus.** Rosenheim<sup>1</sup> describes some cases of typical œsophageal spasm. Suddenly, and apparently without cause, there appears a total inability to swallow. The cardia is firmly closed, but in mild cases it relaxes after repeated deglutitions; in the severer forms they are of no avail. Local anæsthesia or a hypodermatic injection of morphine always produces a relaxation of the spasm, and the cardia remains patent. In most of the cases of dilatation of the œsophagus, Rosenheim, contrary to previous investigators, assumes atony of the œsophagus as the primary factor and not a spasmodic condition. The latter may occur later, due to irritating substances lying above the cardia and inflaming it.

**Stricture of the Œsophagus and Electrolysis.** Aaron<sup>2</sup> describes a new œsophageal electrode, which consists of a rubber stomach-tube closed at its lower end. At this end and at the sides surrounding the tube there are several pin-head openings. A spiral metal electrode is passed through the stomach-tube down to its lower extremity. When the electrode is in the stricture, connection is made through the secretion from the œsophagus, which gathers between the electrode and the tube through the pin-head openings. Electrolysis is applied directly through the stricture. After the œsophageal electrode has entered the stricture it is connected with the negative pole of a galvanic battery. The positive pole is placed on the skin. While both poles are held in position the current should be increased from zero very slowly. Three to five milliampères are allowed to pass through the stricture for ten to twenty minutes. This operation should be repeated three times a week, and a larger electrode should be used at each successive sitting.

According to Aaron, the following points should be observed in sounding the œsophagus:

1. A careful examination should always be made, so that an aneurism may be excluded.
2. A medium-sized soft-rubber stomach-tube should always be the

<sup>1</sup> Ueber Spasmus und Atonie der Speiseröhre. Deutsche med. Wochenschr., Nos. 45, 46, and 47, p. 740.

<sup>2</sup> Stricture of the Œsophagus and Electrolysis by a New Œsophageal Electrode. The Physician and Surgeon, September, 1899, p. 405.

first tube introduced. Smaller ones, down to catgut, can then be used if necessary.

3. Patience will accomplish more than force.

4. If upon the removal of a soft stomach-tube we should find no mucus or blood clinging to the tube, then only is it safe to use stiffer tubes.

5. Trousseau's olive-pointed sounds are valuable in the locating of a stricture.

6. The distance of a stricture from the upper incisors is valuable in locating and determining the cause of the stricture.

7. As soon as a soft tube can be passed through a cicatricial stricture electrolysis can be employed. The negative pole in the stricture, the positive pole on the side of the xiphoid cartilage. Electrodes should be of greater calibre at each successive treatment.

## THE STOMACH.

**Methods of Diagnosis and Treatment.** Krönig<sup>1</sup> and Fürbringer<sup>2</sup> both discovered at the same time that air blown into the œsophagus reaches the stomach without difficulty. They, therefore, recommend the inflation of the stomach, for diagnostic purposes, through the œsophagus. A tube is inserted into the œsophagus reaching to the end of its upper third or to its middle; then air is blown in, either by means of an air suction-bulb or simply by the mouth of the operator. Only in rare instances the air meets with a resistance at the cardia and cannot enter the stomach; in these conditions an abnormal state of the cardia may be suspected. Both authors claim for this method an advantage over the usual method of insufflating the stomach, in that vomiting occurs less frequently and that the procedure is less inconvenient for the patient.

I cannot see any great advantage in this procedure for diagnosis, and think it inferior to the old method of inflating the stomach by pushing the tube directly into this organ; for in the latter, even after inflation, the air easily escapes from the stomach through the tube, while in the new procedure the air will to a greater extent remain in the gastric cavity.

Krönig mentions that he uses the same method for artificial feeding. Here, I think, often a great advantage will be found. In stricture of the œsophagus Krönig first pours in about half an ounce of olive oil, and then liquid food is injected into the œsophagus by means of a cath-

<sup>1</sup> Ueber Injection von Flüssigkeit und Luft in die Magenöhle vom oberen Theil der Speiseröhre aus. Deutsche med. Wochenschr., 1899, No. 44, p. 719.

<sup>2</sup> Deutsche med. Wochenschr., 1899, No. 40.

eter to which a piston syringe is attached. This, however, I do not think is a new method of feeding, as it is already represented by Debove's "gavage," which is done in about the same way.

Fischer<sup>1</sup> endeavored to construct an instrument which should tend to alleviate the difficulty of examination and render it possible to combine at one sitting the various methods, thus arriving at a satisfactory conclusion in a short space of time. The instrument proposed consists of an outer primary tube, through which a gastro-diaphane, an electrode, and an intragastric douche apparatus can be pushed into the stomach. The inner tubes are only one-fifth of an inch thick and provided in their inner part with whalebone, in order to give them the necessary stiffness. I cannot see much gain in this new instrument, for instead of facilitating the *modus operandi*, it seems to me that this arrangement will considerably complicate it.

**Test-meals.** Riegel<sup>2</sup> discusses the subject of the different test-meals and their relative value. As is well known, the test-breakfast of Ewald and Boas and the test-dinner of Leube and Riegel are the two test-meals mostly used. The test-breakfast consists of one cup of tea (without milk or sugar) and one roll; examination of the stomach-contents is made one hour after this meal. The test-dinner consists of a plate of soup, a good portion of meat, potatoes, bread and butter; examination is made three to five hours after this repast. A great deal has been written on the preference of one test-meal over the other. In 1887, I made some investigations on this subject and published them in the *Berliner klinische Wochenschrift*, giving preference to the test-breakfast. Riegel has made new experiments in the same direction, and found that there exist cases in which there is free HCl found after a test-breakfast but not after a test-dinner. He says a stomach may appear to work all right after a test-breakfast, while in reality it performs its function insufficiently after a test-dinner. The fact mentioned by Riegel was also observed by me, and had been mentioned in my paper referred to before. I considered the earlier appearance of free HCl and its easier discovery after the test-breakfast rather as of advantage. Another point of importance I also mentioned in the same article is that after a test-breakfast given in the fasting condition it is easy to recognize admixtures of foods from the previous day, in case there should be any; while this could not be done after the variously composed and complex test-dinner.

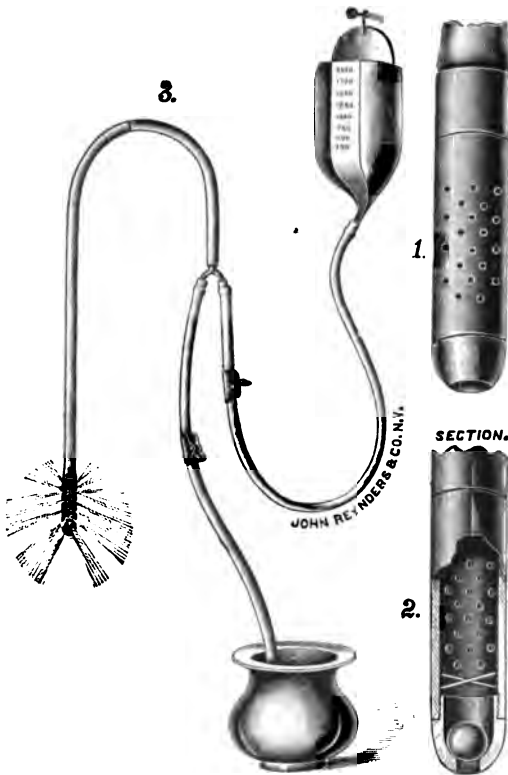
<sup>1</sup> An Arrangement of Gastric Instruments Devised to Facilitate the Physical Examination of the Stomach and its Treatment. New York Medical Journal, December 30, 1899, p. 947.

<sup>2</sup> Zur Prüfung der secretorischen Kraft des Magens. Münchener med. Wochenschr., 1899, No. 45, p. 1489.

**Gastric Douche.** In order to have the action of a douche in the stomach a tube of "a double-current" has to be employed. The double-current tube has the disadvantage that its size is quite considerable, and its introduction into the stomach of the patient is not very convenient.

In order to have an apparatus which could be introduced without any inconvenience, and which would at the same time allow a thorough douching of the stomach, I have constructed a new gastric douche.<sup>1</sup>

FIG. 1.



Its principle is based upon a valve arrangement. The apparatus consists of a rubber tube, not too flexible (thickness, three-eighths of an inch; length, twenty-six inches), at the end of which a hard-rubber capsule is attached (Fig. 1, 1). The latter contains numerous very small openings all around, and one very large opening at its lower extremity. Within the capsule, which can be unscrewed, lies a small aluminium ball. This moves easily and freely within the capsule, and when it lies above the lower opening it entirely occludes the same.

<sup>1</sup> A New Gastric Douche. Medical Record, December 2, 1899.

Two cross-bars in the capsule prevent the entrance of the small ball into the tube (Fig. 1, 2). If the tube described is attached to an irrigator provided with a waste-pipe the apparatus is complete. If the waste-pipe is closed and the water made to run through the douche the liquid will press the ball downward, thus closing up the large opening. The water will then come out through the small side openings like a very fine shower, sprinkling over quite a large area (Fig. 1, 3). The inflowing tube being closed, and the waste-pipe opened while the capsule is inserted into the liquid, the latter will push the ball upward, and thus the large opening will be free, and the water will easily return through it. The liquid will certainly return not only through the large opening, but also through the numerous small side openings. While these, however, do not admit the return of coarse particles, the latter will easily be able to pass through the large hole.

**METHOD OF USING.** The douche end of the apparatus is dipped into warm water and then inserted into the stomach. It is necessary to note that the capsule lies immediately below the cardia, and is not situated deeply in the stomach. The length of tubing from the mouth should be sixteen and one-half to seventeen inches. It may be useful to make a mark at this point of the tube. The tube is now attached to the irrigator, the outflowing pipe closed, the inflowing one opened, and the stomach sprinkled with about a quart of water. In order to make the water return from the stomach the tube is inserted a little further into the stomach (about four to six inches), the outflowing pipe opened and the inflowing one closed. The liquid from within the stomach now returns. This procedure may be repeated three or four times. The temperature of the water should be regulated according to the therapeutic indications. The douche may also be connected with two irrigators, one containing cold, the other warm water; the stomach may thus be sprinkled alternately with cold and warm water.

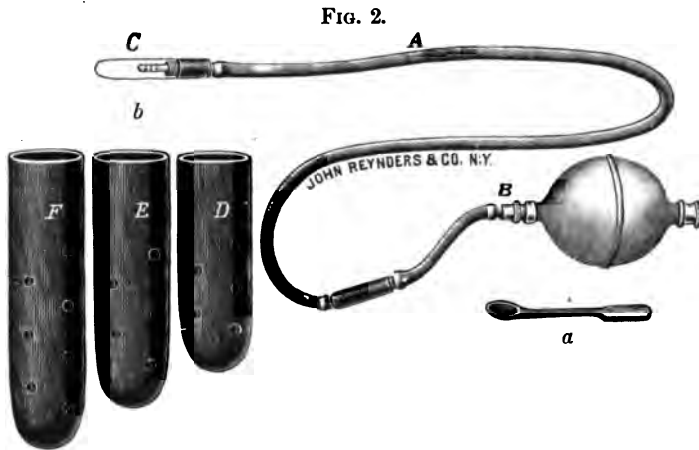
**The Stomach Powder Blower.** By means of the spray only soluble drugs can be applied, but not substances which are either soluble with great difficulty or not at all. In order to facilitate the introduction of the latter I have devised a powder blower for this purpose.<sup>1</sup> The stomach powder blower (Fig. 2) consists of an ordinary, not too flexible, rubber tube (*A*), twenty-eight and a half inches long, the distal end of which connects by means of a hard-rubber piece with an air suction-bulb (*B*), the proximate end of which is attached to a hard-rubber piece (*C*). The latter is hollow and pierced with several small openings at the side for the passage of air, and provided with a screw-thread for the capsule. The capsule (*D*) has numerous holes, and is made in three

<sup>1</sup> New York Medical Journal, April 1, 1899.



different sizes (3, 3½, and 4 cm. long), (Fig. 2, *b*). It is filled with the necessary quantity of powder by means of a very small spoon (Fig. 2, *a*), and screwed on to *C*.

**METHOD.** Insufflation of the stomach with powder can, naturally, be done only when the organ is empty. It should, therefore, be performed in the fasting condition, and, in cases in which the stomach is not empty in the morning, after previous lavage. Proceed as follows: According to the quantity of medicament required, one of the capsules, *D*, *E*, or *F*, is filled with the powder and screwed on to the apparatus; the tube is moistened with warm water and inserted into the stomach; the bulb is then compressed three or four times in quick succession. By holding the ear over the gastric region of the patient during insuffla-



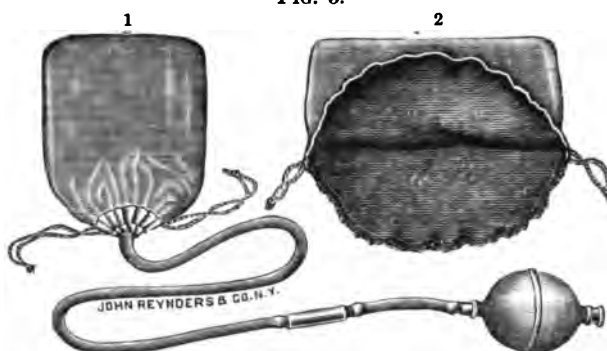
The stomach powder blower. *A*. The tubing part. *B*. Connection with the bulb. *C*. Hard-rubber end with screw-thread for capsule. *b*. The capsule-shaped powder receptacles. *a*. The small spoon for putting the powder into the capsules. *D*, *E*, *F*. Different sized capsules (natural size).

tion the entrance of air (consequently, also, of the powder) is distinctly heard. In cases in which there is much mucus in the pharynx and œsophagus its entrance into the holes of the capsules may be prevented by covering them with vaseline in a thin layer. The latter forms a protecting covering and prevents liquids from coming in contact with the powder. When the apparatus is in the stomach and the bulb compressed the air opens up the vaseline layer over the holes, and the powder can now escape.

The following simple experiment shows that the powder does not collect merely at one spot, but rather spreads over the entire surface of the gastric mucosa: Take a rubber bag (seven inches long and six inches wide), insert the end of the stomach powder blower filled with

powder, and draw the strings together (Fig. 3, 1); then compress the bulb two or three times and remove the insufflator from the bag. If the latter is now opened the powder is found equally distributed upon the entire inner surface of the bag (Fig. 3, 2). This shows that the air disseminates the powder as fine dust over all parts of the inside of the bag. In the stomach the conditions are not different from those in

FIG. 3.



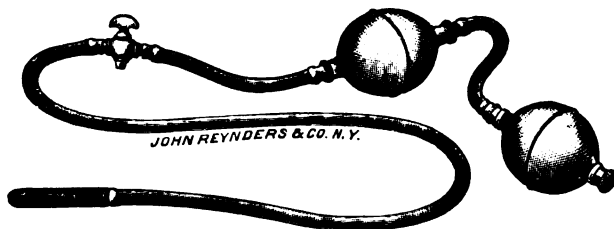
1. A rubber bag with the strings tightened and within the end of the stomach powder blower. 2. The bag opened, the white spots showing the powder.

the bag, and the insufflation of the interior of the gastric cavity with the powder will thus be complete.

*The indications for powdering the stomach* are manifold: In ulcer ventriculi, bismuth; in gastric hemorrhages, antipyrine; in gastralgia, orthoform; and in erosion, protargol can be readily insufflated.

I have recently changed the powder blower for the stomach. The capsule now has three big holes and one small one near the screw-

FIG. 4.



thread. Beside, there is a double bulb with a cock arrangement, instead of the single bulb I formerly used. This modified powder blower (see Fig. 4) acts perfectly, allowing the entire amount of powder within the capsule to be expelled. The capacity of the big capsule is over fifteen grains—i. e., fifteen grains of powder can be thrown into the stomach at once.

**Diet in Hyperchlorhydria and Hypersecretion.** Bachmann<sup>1</sup> has made extensive experiments on twelve patients with regard to the influence of different food substances upon the gastric secretion. In harmony with Pawlow,<sup>2</sup> Jürgensen,<sup>3</sup> Hemmeter<sup>4</sup> and others, Bachmann found that meats produce a more abundant secretion of gastric juice than vegetable foods. Bachmann is of the opinion that vegetable foods (bread, porridge) and milk are more compatible in the affections under consideration than animal foods (meats, eggs). Potatoes he does not consider suitable, as they produce subjective disturbances by the formation of gaseous products and lactic acid. Butter and cream should not only be permissible but their use should be encouraged, as both have a tendency to diminish gastric secretion. As a rule, I allow small quantities of potatoes and meats beside the food substances mentioned by Bachmann, and find practically that the patients get along well.

**Pasteurization of Milk.** Oppenheimer<sup>5</sup> showed that most of the pathogenic germs (especially tubercle bacilli) are killed if exposed to a temperature of 70° C. for ten minutes. Inasmuch as milk undergoes radical changes after its thorough sterilization, and also loses its agreeable taste, Oppenheimer advocates Pasteurization of the milk, at a temperature of 70° C., in preference to sterilization. He has constructed an apparatus for this purpose which does not differ from Freeman's apparatus, used in this country for quite a number of years.

**Poisoning by Potatoes Containing Solanin.** Pfuhl<sup>6</sup> observed a large number of cases of solanin-poisoning among soldiers, who ate, on a holiday, a considerable portion of potatoes. Fifty-six men became sick with very similar symptoms—chills and rise of temperature between 100° and 103° F., headaches, violent colicky pains in the abdomen, diarrhœa, pronounced fatigue, and in some instances vomiting, nausea, and fainting spells. Slight icteric coloration of the conjunctiva and also of the skin was encountered in some of the patients. The fever lasted in most instances about three days, when the patients grew better and recovered.

THE TREATMENT consisted in keeping the patients in bed, the application of an ice-bag over the head, warm fomentations over the abdomen, several doses of calomel (5 grains each), and peppermint tea with tincture of opium.

<sup>1</sup> Experimentelle Studien über die diätetische Behandlung bei Superacidität. Archiv f. Verdauungskrankheiten, Bd. v., Heft 3, p. 336.

<sup>2</sup> Die Arbeit der Verdauungsdrüsen, Wiesbaden, 1898

<sup>3</sup> Arch. f. Verdauungskrankh., 1898, Bd. iii., Heft 2.

<sup>4</sup> Diseases of the Stomach, Philadelphia, 1898.

<sup>5</sup> Ueber das Pasteurisiren der Milch zum Zwecke der Säuglingsernährung. Münch. med. Wochenschr., 1899, No. 4.

<sup>6</sup> Ueber eine Massenerkrankung durch Vergiftung mit stark solaninhaltigen Kartoffeln. Deutsche med. Wochenschr., November 16, 1899, p. 753.

Pfuhl had some of the potatoes examined, and they were found to contain 0.38 per cent. of solanin, or about six times the amount usually found in them.

**The Milk of Nursing Women.** Pletzer<sup>1</sup> has made several experiments with regard to influencing the quality of milk of nursing women, and found that abundant nutrition increases the secretion of milk. The addition of tropon (30 grammes, or 1 ounce, per day) or some other preparation of albuminoid food to the diet increases the quantity of fat in the milk, while the albumin remains unchanged. He arrives at the conclusion that a diet rich in albuminous foods exerts a beneficial influence on the mother as well as on the child during the period of lactation.

**Bread and Butter.** Hemmeter<sup>2</sup> gives a detailed description of the way bread is made, and speaks of the great value of bread and butter in the diet: "Here the most modern physiology has given an instructive explanation of the instinct by which the human race has for ages been led to associate bread and butter. We all know that fats cannot be digested very well in an acid medium. It is also known that carbohydrates, such as bread, which contains on an average between 50 and 60 per cent. of starchy matter, cannot be digested very well in an acid medium.

"Fatty foods are difficult to digest, and those afflicted with weak stomachs must avoid them. If fat is present in the gastric chyme to any considerable extent it arrests the secretion of acid gastric juice in its own interest, and in that way impedes the digestion of the albuminous or proteid bodies. For that reason the combination of fatty and albuminous food is difficult of digestion, and only agrees with people who have a strong stomach and an intense appetite, the explanation being that the albuminous food requires an acid medium for its solution in the stomach and actually stimulates the acid secretion, whereas the fats require an alkaline medium and depress the acid secretion. The combination of bread and butter is not difficult of digestion, because the bread contains comparatively little proteid or albuminous matters—from 6 to 12 per cent. on the average—and, therefore, it requires little acid for its digestion; hence, the fat (butter) in depressing the acid secretion favors the transformation of the large percentage of starch in the bread into maltose and dextrose. On the other hand, the fat is a stimulant to the secretion of the pancreas, and thus an abundance of ferments is secreted into the duodenum, and secures the digestion of the starch as well as the albumin and fat."

<sup>1</sup> Zur Ernährung stilleuder Frauen. Münchener med. Wochenschr., 1899, No. 46, p. 1529.

<sup>2</sup> Dietetics of Bread and Butter. Maryland Medical Journal, February, 1900, p. 61.

In my article on "The Diet of Dyspeptics"<sup>1</sup> I have laid great stress upon the importance of bread and butter. I cite the following as of interest:

"Bread forms one-third of the total amount of ingested food in health, and, beside having nutritive value, serves the purpose of increasing the flow of saliva during its mastication. It also creates an appetite for other food.

"Butter not only improves the taste of various kinds of food, but is also in itself a nutriment of the greatest importance. The great number of calories which butter contains (100 grammes give 837 heat units, while the same amount of bread develops about 217) shows this in the clearest manner. Another advantage which butter presents is that its volume is only about one-third that of bread. A patient taking about one-quarter of a pound of butter a day receives therewith more than one-half of the heat units required. This quantity of butter is, according to my experience, well borne by most patients."

**Shape and Position of the Stomach.** Bettman,<sup>2</sup> in examining the shape of the stomach by inflation in autopsies, discovered the remarkable fact that the cardiac orifice is invariably much nearer the anterior than the posterior wall. This asymmetry of insertion is constantly present, occurring in all stomachs, both foetal and adult. It may, however, vary in degree. In general, Bettman found that about two-thirds of the fundus lie behind the cardiac orifice and one-third in front.

With regard to enteroptosis, Bettman follows the lines of Glénard and others. He is, however, against the use of the abdominal bandage, especially in young women, as it has a tendency to weaken the abdominal muscles.

**Erosions of the Stomach.** L. Sansoni<sup>3</sup> has described, under the name of "gastritis ulcerosa chronica anachlorhydrica," a new disease, characterized by gastric pains, the appearance of small fragments of the mucous membrane of the stomach in the wash-water of this organ in the fasting condition, and the absence of free HCl.

In my opinion the disease in question is nothing more than "erosions of the stomach"—a condition which was first clinically described by myself, and which has been found to exist pathologically in many autopsies. I differ from Sansoni, inasmuch as I found erosions of the stomach also in cases accompanied by a normal gastric juice and by hyperchlorhydria.

<sup>1</sup> The Diet of Dyspeptics. Medical Record, January 1, 1898.

<sup>2</sup> The Shape and Position of the Stomach. Philadelphia Monthly Medical Journal, March, 1899.

<sup>3</sup> Ueber die Gastritis ulcerosa chronica anachlorhydrica. Arch. f. Verdauungskrank., 1900, Bd. vi., p. 1.

**Gastric Ulcer.** Greenough and Joslin<sup>1</sup> have made a statistical study of all the cases of gastric ulcer occurring in the years 1888 to 1898. Among 13,097 cases there were 187 cases of gastric ulcer. The frequency of the chief symptoms was as follows :

|                             | Cases. | Per cent. |
|-----------------------------|--------|-----------|
| Vomiting . . . . .          | 179    | 95.7      |
| Pain . . . . .              | 173    | 92.5      |
| Vomiting of blood . . . . . | 147    | 78.6      |
| Pallor . . . . .            | 131    | 70.1      |
| Tenderness . . . . .        | 130    | 69.5      |
| Constipation . . . . .      | 123    | 65.8      |

With regard to treatment, starvation diet and rectal feeding were the therapeutic measures adopted in the more severe cases, and a milk diet was given, as a rule, in the milder ones, so that a comparison of the two forms of treatment can hardly be made with justice. It may be said, however, that while on one service the rectal feeding was more popular, and on the other the milk diet was the rule, the percentages of recovery on the two services were the same.

The writers summarize their conclusions as follows :

1. Gastric ulcer is more frequent in Boston than in Chicago, Baltimore, or Denver.

2. It is five times as common in women as in men.

3. The average age in men is thirty-seven years ; in women twenty-seven.

4. Hemorrhage was present in 81 per cent. of the cases. It caused the death of 17 per cent. of the male patients, but only 1.27 per cent. of the females. No woman under thirty years died of hemorrhage from gastric ulcer during this period.

5. The blood was that of a chlorotic type of anæmia.

6. Perforation occurred in 3.2 per cent. of the cases, and none of these patients left the hospital alive.

7. Of 114 patients 80 per cent. were discharged cured or relieved, but at the end of an average period of five years only 40 per cent. remained well. The mortality at the same time (due to gastric disease) was 20 per cent. Among the males it was 30 per cent. ; with the females 9 per cent.

8. The excessive mortality of ulcer among men, its occurrence in life a decade later than in women, and the absence of fatal cases of hemorrhage in females, point to a difference of the ulcer in the two sexes.

9. The mortality of 8 per cent. and the failure of medical treatment to effect a lasting cure in 60 per cent. of the patients indicate the need of surgical intervention in other than emergency cases of this disease.

<sup>1</sup> Gastric Ulcer at the Massachusetts General Hospital, 1888-1898. Boston Medical and Surgical Journal, vol. cxli., No. 16, p. 389.

It seems to the writer that the relative proportion of ulcer in the two sexes, namely, in females five times as often as in males, found among the patients of the Massachusetts General Hospital cannot be generalized.

**Cancer of the Stomach.** Osler and McCrae<sup>1</sup> report six cases of cancer of the stomach in patients under thirty years of age. The striking features of these cases are the abruptness of the onset and the acuteness of the course. The duration is, as a rule, between two and six months. The authors corroborate two of Mathieu's conclusions, namely :

1. Cancer of the stomach below the age of thirty years has generally a rapid progress, and often ends suddenly by incidents more or less abrupt.

2. Early cancer is not latent ; it is overlooked.

**THE BLOOD IN CANCER OF THE STOMACH.** Krokiewicz<sup>2</sup> has examined the blood in seventeen cases of cancer of the stomach and arrived at the conclusion that the hæmatological findings in cancer are quite different. They do not represent any positive characteristic signs of the cancerous affections. With regard to the cachexia encountered in cancer of the stomach, Krokiewicz ascribes it to a blood-intoxication originating from abnormal faulty products of metamorphosis.

**Acute Dilatation of the Stomach.** After giving a thorough review of the literature on this subject, Bettman<sup>3</sup> describes a case of dilatation of the stomach, with recovery, which he observed himself. He gives the following description of the case :

"B. L., aged seventeen years, of Russian extraction, very well developed and nourished, was admitted to my service in the Jewish Hospital, October 23, 1895. She was in perfect health up to two weeks prior to admission, at which time the prodromal symptoms of typhoid fever began. On admission she presented a typical picture of typhoid fever, including the rose spots and enlargement of the spleen. The only serious complications were vomiting, which occurred one or more times daily, and retention of urine, requiring catheterization throughout the whole course of her illness. During the first fifteen days after admission the disease progressed naturally ; she was delirious at times, vomited frequently, and complained of abdominal tenderness. Convalescence was fully established by November 13th, at which time she felt very hungry and took nourishment well.

<sup>1</sup> Cancer of the Stomach in the Young. New York Medical Journal, April 21, 1900, p. 581.

<sup>2</sup> Das Verhalten des Blutes im Verlaufe von Magencarcinom. Arch. f. Verdauungskrankh., 1900, Bd. vi., p. 25.

<sup>3</sup> Acute Dilatation of the Stomach. Philadelphia Medical Journal, February 3, 1900.

"On November 13th she vomited once, but felt well.

"On the 14th she complained of severe abdominal pain, became very nervous, being delirious at times, and vomited eight times. Food was stopped. The abdomen was enlarged and tender.

"On the 15th the restlessness continued until 10.30 P.M., when she suddenly collapsed. Her temperature fell to 96.5° F.; she was pulseless at the wrist.

"It was with the greatest difficulty that she was kept alive during the next day, during which time she was pulseless and cold, and vomited large quantities of a thin, greenish fluid. Occasionally she would swallow a small quantity of cracked ice with a few drops of chloroform, but for the most part her sensorium was dulled. Her bowels moved spontaneously, the stool being brown and watery. About 700 c.c. of urine were drawn during the twenty-four hours. During the day she vomited twenty to twenty-five times, the quantity of fluid varying from 25 to 150 c.c. each time. The total quantity must have been nearly three pints.

"On the 17th the vomiting continued unabated, the fluid, of light green color, coming up in large quantities. Her bowels moved three times spontaneously. Her abdomen was still distended. The condition of collapse continued, though the patient was conscious throughout the day.

"On the 18th the condition of the patient was so desperate that gastric lavage, presumably as a last resort, was determined upon. A very thin tube was passed without much difficulty, and a large quantity of thin, greenish fluid was removed. The condition of the patient improved almost immediately, the abdominal distention disappeared, the sensorium became clearer, and rectal alimentation was resorted to. The vomiting ceased for about eighteen hours. The bowels moved spontaneously, the stools being thin and brown.

"Gastric lavage was practised once or twice daily for three days, and the patient was nourished entirely by enemas for five days. Her convalescence was slow. She vomited at times and remained weak, being slightly delirious now and then.

"On the 21st she retained some iced tea and orange-juice. From the 22d on her improvement was more rapid; her stomach retained koumyss, buttermilk, chicken-broth, and her strength slowly returned. She remained in the hospital two months more, suffering from ulcers on the legs due to sloughing in places where ether had been injected."

The diagnosis of acute dilatation of the stomach in this case, which was based on the very violent and incessant vomiting, the collapse, and the distention of the abdomen, does not appear to me sufficiently proven, for there are several intestinal lesions which can bring on similar symp-



toms without the existence of a severe lesion of the stomach. In fact, the frequent vomiting of small quantities (25 to 100 c.c.) of fluid, principally bile, and the very rapid recovery, militate, in a certain measure, against the diagnosis of acute gastric dilatation.

**Atonic Dilatation of the Stomach.** Musser and Steele<sup>1</sup> describe eight cases of atonic dilatation of the stomach, mostly in young people studying hard, and arrive at the following conclusions :

1. The symptoms upon which most reliance can be placed in determining the presence of gastric motor insufficiency are : (a) The presence of fluid and food in the stomach fasting overnight ; (b) the ready entrance of fluid through the tube and difficulty in the return flow ; (c) the absence of visible gastric peristalsis ; (d) evidences of fermentation and intoxication by the products thereof ; (e) thirst and (f) scanty and concentrated urine.

2. In determining the position and size of the stomach, by far the most certain method has been inflation by air through the stomach-tube ; auscultatory percussion, Dehio's method, and determining the capacity of the stomach by the amount of water required to produce a sense of fulness, while signs of value may lead to error.

3. It may be inferred from the somewhat small number of cases just reported that the condition is not uncommon in students. An analysis of the etiological factors is as follows : (a) Myasthenia caused by chronic gastritis from the abuse of alcohol and tobacco, four cases ; (b) myasthenia from deficient innervation, two cases ; (c) myasthenia, probably of congenital origin, one case ; (d) myasthenia occurring in the course of acute disease, one case.

Turck,<sup>2</sup> who discusses the same subject, gives the following directions for the treatment of motor insufficiency combined with pronounced hyperchlorhydria :

"Withdraw all food from the stomach for a time and give the organ a prolonged period of rest. Give food by the rectum twice a day and water by the rectum for one week, giving in addition subcutaneous injections of physiological salt solution.

"In the second week give food by the stomach once every other day, continuing the rectal feeding.

"During the third week give food by the stomach once a day, still continuing the rectal feeding.

"In the fourth week give two meals a day, and continue gradually to increase until the normal condition is reached.

<sup>1</sup> Some Cases of Dilatation of the Stomach. American Journal of the Medical Sciences, February, 1900, p. 125.

<sup>2</sup> Motor Insufficiency of the Stomach. Chicago Clinical Review, March, 1900.

"All food should be reduced to as finely divided a condition as possible, and little liquid should be given."

**Hypertrophic Pyloric Stenosis in Infancy.** Pritchard<sup>1</sup> gives a detailed account of all the cases of pyloric stenosis in infancy mentioned in the literature, and adds one new case of his own, which he describes as follows :

"Healthy male child; born at full term of healthy parents, weighed nine pounds, and had one healthy elder brother living. It was fed by hand, and looked after by the monthly nurse for the first three weeks of life; it was not seen by the doctor in attendance, as it appeared to be doing well. The quantity of food (diluted milk) given was stated to be the bottle full (five ounces) every three or four hours. During the first three weeks there were no symptoms except sweating, which was profuse, but the weather was very hot, and might have accounted for it. At the third week vomiting set in; the urine was very scanty and the bowels constipated; the amount of food was reduced and bismuth and soda given. In spite of treatment the symptoms continued and the child persistently lost weight, until at the seventh week it weighed only six pounds. At this period it was brought up to London and placed under Dr. Cheadle's care, and from then until the time of its death I had an opportunity of watching it together with Dr. Cheadle. Examination showed that it was emaciated to an extraordinary degree, face pinched and anxious, bones small, and fontanelles normal, but slightly depressed; lungs and heart normal; tongue and fauces remarkably clean; the abdomen was flaccid and carinated, and the vertebral column was easily palpated through the abdominal walls; there were no enlarged mesenteric glands; the upper part of the abdomen was more prominent and resonant to percussion. At times the outline of the stomach was quite evident, and extended as far as or below the umbilicus. Carefully watched, slow waves of contraction could be distinguished passing from left to right, the time occupied being from three to four seconds from the time of commencement at the cardiac end to its disappearance at the pylorus; occasionally, however, the wave of contraction would remain stationary for some seconds midway between its commencement and its completion, giving the stomach an hour-glass-shaped appearance. No tumor or sense of resistance could be made out at the pylorus. The temperature was normal. On the day following my first examination the child was driven from South Kensington in a closed carriage to see Dr. Cheadle at his house, but while in his consulting-room it was seized with convulsions, and the temperature rose to 104.5° F., and the respira-

<sup>1</sup> Hypertrophic Pyloric Stenosis in Infancy. Archives of Pediatrics, April, 1900, p. 241.

tions were of the Cheyne-Stokes character. A few hours after it had been taken home I saw it again. It was then apparently moribund, but recovered somewhat after an enema of Valentine meat-juice and brandy. By nutrient enemata and teaspoonful quantities of food by the mouth it not only maintained life, but seemed to put on weight and gain in strength, and all vomiting had ceased. But on the tenth day after its arrival in town the head became retracted, there were external strabismus, hiccough, deviation of the head to the right, and carpopedal contractions; indeed, the nails of the hands were driven into the palms, and pads of lint had to be interposed. With these symptoms there was marked inco-ordination in the act of deglutition, and practically nothing could be swallowed, and the enemata, which up to now had been well retained, were immediately rejected. Two days later the child died.

"At the autopsy the brain and meninges were found slightly congested and the lateral sinus distended. All the other organs appeared healthy and normal. The œsophagus was dilated throughout, especially at its junction with the stomach. The stomach was enlarged and capable of containing about seven ounces of water. The walls were slightly thickened, especially at the pyloric end. At the pylorus itself was a hard, annular thickening, giving almost the appearance of the impaction of some foreign body about the size of a large filbert nut. A No. 5 catheter could just pass through the opening. On slitting the pylorus open the walls were found to be enormously thickened, and to consist of a pale, homogeneous tissue. Microscopically, the circular muscular layer was found to be greatly hypertrophied, but beyond this there was nothing abnormal in the structure."

As a *résumé* of his valuable paper, Pritchard gives the following conclusions:

1. That the hypertrophy is secondary to overaction of the sphincter and the stenosis chiefly due to spasm.
2. That the stenosis as measured post-mortem is but an accurate gauge of its organic degree during life.
3. That overaction and inco-ordinated contractions of the sphincter may be due to some fault in the nervous mechanism.
4. That injudicious feeding, either quantitatively or qualitatively, may be a contributory factor of the nervous inco-ordination.

**Sweet Oil in the Treatment of Ischochymia Caused by Pyloric Stenosis.** Cohnheim<sup>1</sup> reports a case of traumatic ulceration of the stomach, followed by pyloric obstruction and the symptoms of ischochymia. Upon the advice of a lay friend the patient took a wineglassful of sweet oil, twice daily, half an hour before breakfast and supper, and

<sup>1</sup> Ueber Gastrectasie nach Traumen. Arch. f. Verdauungskr., 1899, Ed. v., p. 405.

quickly recovered from all his severe symptoms. Cohnheim, therefore, suggests the oil as a remedy to be tried in this and similar affections of the stomach accompanied by hyperchlorhydria.

I had the opportunity of making use of olive oil (3 to 4 ounces), taken three times daily, half an hour before meals, in a case of ischochymia, with good results.

**Achylia Gastrica Simulating Hyperchlorhydria.** In a paper which has appeared in the *Jacobi Festschrift*,<sup>1</sup> I described cases of achylia which, as regards their subjective symptoms, are almost typical of hyperchlorhydria. In the latter disease the disturbances (pains, distress, feeling of fulness, etc.) appearing usually one or two hours after meals, are caused by too great acidity of the gastric contents. At first sight it seems rather strange that we should encounter the same symptoms in cases of achylia gastrica—i. e., where there is practically no gastric juice, and hence no acid present. Still this is so, as can be seen from my observations.

In my book on *Diseases of the Stomach* I have already mentioned that pyrosis may be met with in achylia gastrica. Martius,<sup>2</sup> in his book on *Achylia Gastrica*, likewise cites a case of achylia in which the principal symptoms were constipation and a burning sensation appearing in the gastric region soon after meals, and lasting from half an hour to one hour. In these cases the burning sensation and other symptoms found in hyperchlorhydria (pains, distress, etc.) are certainly not due to irritation of the gastric mucosa by acid substances, for these are entirely absent. It may be that the coarser particles of food, especially after the escape of fluids from the stomach, which occurs in achylia at an early period after meals, excite the mucous membrane mechanically in an intense manner by rubbing against it, and this may be felt as burning or pain. That the ingestion of water would ease this sensation is quite evident. The added fluid mingles with the solid particles lying in the stomach, and thus lessens the mechanical irritation. But why the addition of food (even solid substances) should give relief to the pain and burning in some of these cases requires further explanation. It may be that the act of eating, as such, fully occupying the mind, draws the attention away from the stomach, and, therefore, the pain or discomfort is allayed (in reality forgotten).

Cases of achylia gastrica presenting subjective symptoms almost identical with hyperchlorhydria are not very rare. I have observed six cases of this type during the present year. Two of these cases were almost typical of hyperchlorhydria; in both there were pains about two hours after meals, and these disappeared after the ingestion of food or

<sup>1</sup> Achylia Gastrica Simulating Hyperchlorhydria. *Jacobi Festschrift*, New York, 1900.

<sup>2</sup> *Achylia Gastrica*, 1897, p. 55.

drink. Two other cases showed the period of pain and burning sensation as early as half an hour after meals. While this is not the rule for hyperchlorhydria, in many cases of this disease, however, especially if it is very marked, the pains appear just as early. The fifth case suffered from pains two to three hours after meals, which were followed by diarrhoea. The latter symptom is not exactly characteristic of hyperchlorhydria, but is met with occasionally there also. In the sixth case the pains appeared half an hour after meals, lasted about two hours, and were combined with dizziness. This symptom I have also now and again met with in hyperchlorhydria, although, as a rule, somewhat later after meals. In all the six cases described the distress, burning, or pains promptly disappear after the ingestion of food. This circumstance is the most characteristic feature of hyperchlorhydria, and we find it here also.

THE DIAGNOSIS in these cases has been made after repeated examinations of the gastric contents, which showed the characteristic features of achylia gastrica.

Several of these patients, particularly the first two, who were physicians, had at first treated themselves for hyperchlorhydria, but without deriving any benefit. After the correct diagnosis had been established they improved very promptly.

The importance of examination of the gastric contents for diagnostic purposes is evident from the above observations.

The prognosis of this special variety of achylia is not different from that of other forms of achylia gastrica, and is good unless grave complications, especially of the intestine, develop. As a general rule, improvement is observed. As a matter of fact, all my cases during this year were benefited by appropriate treatment to such a degree that they finally presented almost no subjective symptoms whatever.

Beside the usual treatment of achylia, the cases described require special attention for their hyperchlorhydric symptoms. The use of water (half a glassful or a glassful) about one or two hours after meals, just at the time the distress is experienced, appears to be very rational. The water acts as a diluent and diminishes the rubbing of solid particles against the gastric walls (as already mentioned above). Experience teaches that in many of these cases this simple remedy brings relief. In a few instances milk and crackers were given between meals also with benefit. If these measures are not sufficient the bromides will then be found useful, bromide of sodium or strontium being given in twelve-grain doses twice daily.

**Syphilis of the Stomach.** Dyspeptic symptoms not infrequently occur in the secondary and tertiary stages of syphilis. While in the secondary stage, however, the digestive disturbances are attributable to

the constitutional condition, to the fever, etc., and hence are to be regarded as concomitant phenomena of the original disease, without any special involvement of the stomach, the affections of the stomach in the tertiary stage of syphilis are of independent nature, caused by anatomical processes in that organ.

The lesions of the stomach during the tertiary stage of syphilis may assume various forms (erosions, ulcers, tumors, stenosis of the pylorus, gastralgia, etc.), all of which present the features of the ordinary types of these affections; their syphilitic nature cannot be recognized by the symptoms alone. Diagnosis of their syphilitic origin is facilitated, first, by the demonstration of a previously existing luetic infection; second, by syphilitic manifestations in other portions of the body; and, third, by the successful results of antisyphilitic treatment.

It is scarcely necessary to mention that syphilitic subjects may suffer from any of the diseases of the digestive tract without there being any connection between the latter and antecedent lues. Indeed, these cases probably constitute the majority. Hence, it is the more difficult to decide in any given case whether the disease of the stomach is of a syphilitic nature or not. Yet this is quite often possible.

Syphilis of the stomach has been observed by Andral,<sup>1</sup> Wagner,<sup>2</sup> Lancereaux,<sup>3</sup> Cornil,<sup>4</sup> Chiari,<sup>5</sup> Stolper,<sup>7</sup> Gaillard,<sup>8</sup> Mracek,<sup>9</sup> Osler,<sup>10</sup> Hemmeter,<sup>11</sup> Dieulafoy,<sup>12</sup> Fournier,<sup>13</sup> Flexner,<sup>14</sup> Mackay,<sup>15</sup> Fraenkel,<sup>16</sup> Aristoff,<sup>17</sup> and myself.<sup>18</sup>

<sup>1</sup> Clinique Médicale, Paris, 1834, t. ii., 99, 201-207.

<sup>2</sup> Das Syphilom, oder die constitutionelle syphilitische Neubildung. Archiv f. Heilkunde, Bd. iv., p. 225.

<sup>3</sup> Traité de la syphilis, 1866, p. 406.

<sup>4</sup> Leçons sur la Syphilis, Paris, 1879, p. 406.

<sup>5</sup> Lues hereditaria mit gummöser Erkrankungen des galleleitenden Apparates und des Magens. Prager med. Wochenschrift, 1885, No. 47, S. 461.

<sup>6</sup> Ueber Magensyphilis. Festschrift f. R. Virchow, 1891, ii., p. 297.

<sup>7</sup> Beiträge zur Syphilis visceralis. Bibliotheca Medica, 1896, Bd. c., Heft 6.

<sup>8</sup> Archiv général de médecine, 1896, i., p. 66-83.

<sup>9</sup> Lehmann's med. Handatlanten, Bd. vi., Syphilis und venerische Krankheiten. München, 1898, p. 52.

<sup>10</sup> The Principles and Practice of Medicine, New York, 1891, p. 178.

<sup>11</sup> Diseases of the Stomach, 1897, p. 556.

<sup>12</sup> Syphilis de l'estomac. Bulletin de l'académie de médecine, 1898, No. 20, p. 578.

<sup>13</sup> Cited by Dieulafoy, loc. cit.

<sup>14</sup> Gastric Syphilis, with Report of a Case of Perforating Syphilitic Ulcer of the Stomach. American Journal of the Medical Sciences, 1898, N. S., cxvi., p. 424.

<sup>15</sup> The Role of Syphilis in the Etiology of Simple Ulcer of the Stomach. Lancet, 1898, ii., p. 1701.

<sup>16</sup> Zur Lehre von der erworbenen Magen-Darm Syphilis. Virchow's Archiv, 1899, Bd. 155, p. 507.

<sup>17</sup> Zur Kenntniss der syphilitischen Erkrankungen des Magens bei hereditärer Lues. Zeitschrift f. Heilkunde, 1898, xix., p. 395.

<sup>18</sup> Syphilis of the Stomach. Philadelphia Medical Journal, February 3, 1900.

Among the cases which I have observed it is best to differentiate three groups of syphilitic diseases of the stomach, namely :

1. Gastric ulcer of syphilitic origin.
2. Syphilitic tumor of the stomach.
3. Syphilitic stenosis of the pylorus.

The following two cases belong to Group 1. (Gastric ulcer of syphilitic origin.)

Group 1 (syphilitic ulcer of the stomach) is chiefly represented clinically in the literature. I have observed two cases belonging to this class. In the first case other signs of tertiary syphilis existed, while in Case 2, aside from the lesion of the stomach, nothing further of a luetic nature could be found. In both cases the customary methods of treatment of gastric ulcer were entirely or partially unsuccessful, while anti-syphilitic therapy was followed by complete recovery.

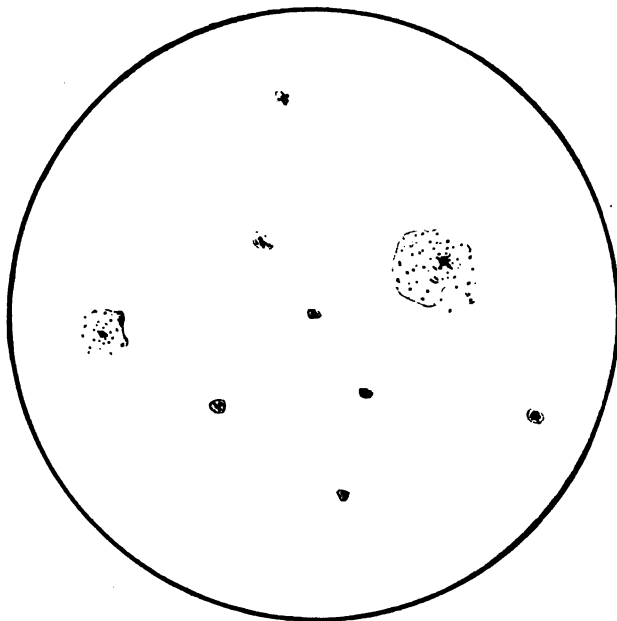
The second group (syphilitic tumors of the stomach) has received but scant mention in the literature, as far as I have been able to learn, except in a few reports of autopsies, but has not been described as having been recognized during the lifetime of the patient. I have described two cases belonging to this group. The occurrence of syphilitic tumors of the stomach is quite rare, but none the less important. They may run their course in a manner similar to carcinoma, and readily be mistaken for the latter. On palpation such a gummatous tumor may evince all the characteristics of a malignant neoplasm, and even the symptoms may so strongly resemble those of cancer as to be confounded with the latter. It would appear, therefore, advisable in every case of neoplasm of the stomach to bear in mind the possibility of syphilis, and to question the patient as to any previous history of that disease and examine for any other syphilitic manifestations on the body.

The third group of syphilitic pyloric stenosis is of great practical import. In one of the cases I have observed a thickened pylorus could be felt as an oval tumor which disappeared under continued anti-syphilitic treatment. At the same time the symptoms of isochymia receded and the patient recovered. In a second case the pylorus was not palpable, and the diagnosis of the commencing constriction had to be based upon the results of internal examination of the stomach. In both cases the customary medical measures indicated in benign pyloric stenosis proved insufficient, while the administration of potassium iodide soon effected the improvement.

From the remarks just made it appears distinctly that tertiary syphilis may produce severe gastric affections which are susceptible to antiluetic treatment. In the therapeutics of intractable diseases of the digestive apparatus, therefore, the possibility of a syphilitic origin of the trouble must never be forgotten.

**Mould in the Stomach and its Probable Significance.** The part which micro-organisms (bacteria and mould fungi) play in the occurrence of pathological processes in the stomach has been variously interpreted by authors. Most clinicians ascribe no special significance to them. Others, however, assign them a prominent place; thus, for example, Talma<sup>1</sup> maintains that the fermentation of carbohydrates induced by micro-organisms is the cause of hyperchlorhydria; others, again, place stress not so much upon the variety of these microbes as upon their ultimate number.

FIG. 5.



Small pellicles of mould found in the stomach. (Natural size.)

In the literature scant references to mould fungi in the stomach are found which relate to the findings of microscopical examinations. Mould itself, recognizable by macroscopical examination, has, according to my knowledge, not as yet been observed clinically in the stomach. I have had occasion to observe several cases of mould formation in the stomach.<sup>2</sup> In these there were found in the wash-water of the empty stomach small, sometimes blackish-gray and sometimes brownish-green flakes (2 to 5 mm. in diameter; see Fig. 5) in varying numbers (four to fifty and more). The microscopical examination showed that these

<sup>1</sup> Von der Gärung der Kohlehydrate im Magen. *Zeitschr. f. klin. Medicin*, 1898, Bd. xxxv., p. 542.

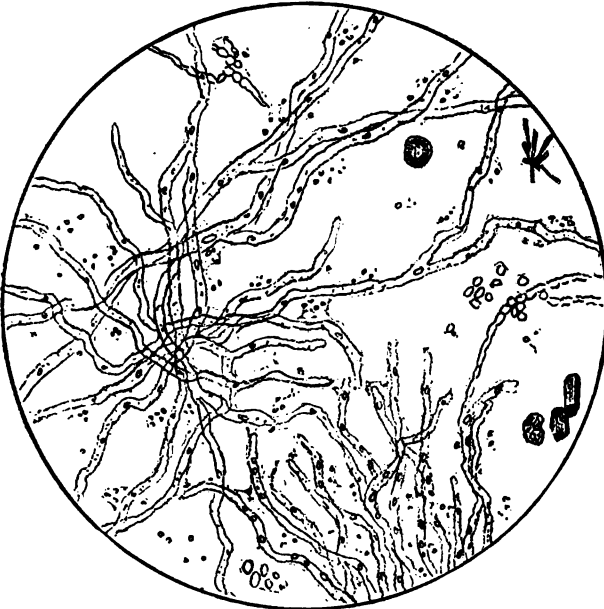
<sup>2</sup> The Occurrence of Mould in the Stomach and its Probable Significance. *Medical Record*, June 16, 1900, p. 1025.



flocculi consisted entirely of spores and mycelia and scarcely anything else. Similar flocculi were found in the same patients in the gastric contents after a test-meal, and the microscope showed the same picture as in the flocculi from the empty stomach.

Sometimes these blackish-gray masses are embedded in mucus. We then note beside these fungous colonies mucous corpuscles and numerous epithelial cells. This indicates an intimate connection between the fungous colonies and the surface of the mucous membrane. The former must adhere quite closely to the latter and perhaps even proliferate into the epithelial layer. This firm adhesion must be assumed for the fol-

FIG. 6.



A greenish pellicle found in the wash-water of the stomach (of Wm. R.), in the fasting condition. Mycelia, free spores, and a few crystals are visible.  $\times 240$ .

lowing reasons: If the fungi were only an accidental admixture of the ingesta—that is, introduced with the latter and then carried further onward, without there being any fungous proliferation—then they would be encountered only in the gastric contents after meals, but not in the fasting state of the patient—that is, when no food is found. As a matter of fact, however, in the cases referred to these flocculi occur in large numbers, principally in the empty stomach.

Are these mould fungi present in the stomach still in a living condition or are they destroyed by the action of the gastric juice? In answer to this question it can be said that the mould colonies retain

FIG. 7.

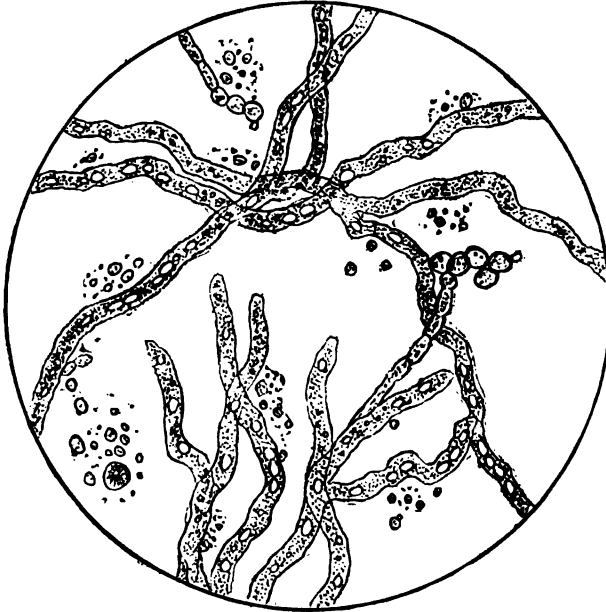
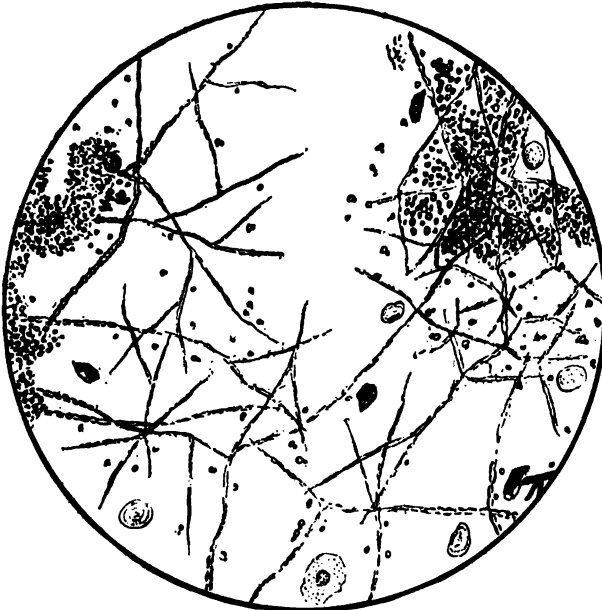
Same as Fig. 6, highly magnified.  $\times 420$ .

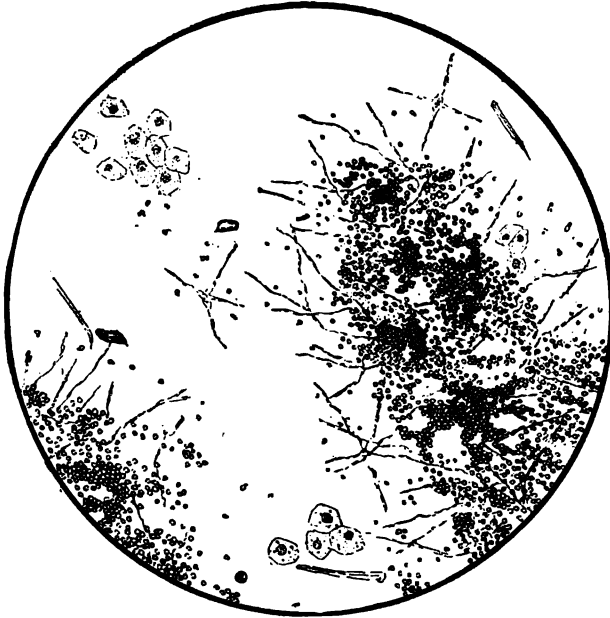
FIG. 8.



A blackish pellicle found in the gastric contents (of T. M.) after a test-breakfast. Numerous spores, mycelia, a few crystals, starch granules, and epithelial cells are visible.  $\times 140$ .

their full vitality and are capable of further development. If the flocculi are placed in some water or in the filtrate of the gastric contents

FIG. 9.



A blackish pellicle found in the wash-water of the stomach (of L. C.), in the fasting condition. Numerous spore colonies, mycelia, a few crystals, epithelial cells, and several algae are visible.  $\times 120$ .

FIG. 10.



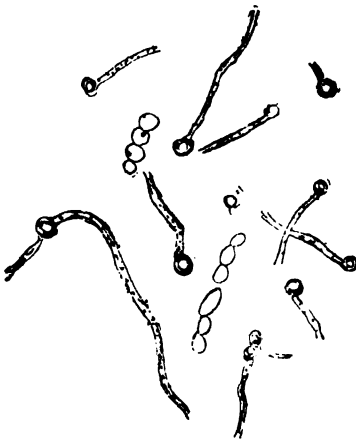
Showing mycelia and spores. Oc. 2. Obj.  $\frac{1}{12}$  oil, Leitz.

of the patient it is soon noticed that there is a formation of whitish-gray clouds which are connected with the flocculi, and under the microscope we find spore colonies and mycelia very similar in character to the original mould.

Dr. E. K. Dunham has identified the mould as *penicillium glaucum*.

What significance have these mould fungi in gastric pathology? Although isolated fungi may exist in the stomach for a short time without any detriment, they do not find in the normal organ favorable soil for further development. They are intimately mixed with the chyme and are carried onward, living or dead, through the pylorus. Entire colonies of fungi which are macroscopically perceptible are probably never to be found in the normal stomach. Any considerable growth of

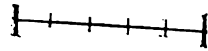
FIG. 11.



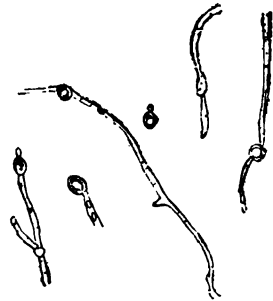
Showing mycelia and spores.

Oc. 2. Obj.  $\frac{1}{12}$  oil.

FIG. 12.



Scale, 0.05 mm. Each division = 0.01 mm.



Same as Fig. 11. Oc. 2. Obj.  $\frac{1}{12}$  oil.

mould would be possible only if a colony of the fungi had infested a fold of the surface of the gastric mucous membrane and had become so firmly adherent that they were not carried along with the onward passage of the chyme. Under these circumstances a fungous colony may grow undisturbed, and considerable areas of the gastric mucosa may become covered with mould. In the above-described cases such a condition must have prevailed. In lavage of the stomach the inflowing current of water exerts considerable force and tears many mould islets from their bases, so that they then appear in the wash-water.

It is scarcely conceivable that such a mould coating of certain zones of the gastric mucosa can be unattended with disturbances of the functions of the organ. Conditions of irritation as well as inflammatory

processes might be expected *a priori* from the mechanical action of the mould.

After these theoretical conclusions it would be profitable to analyze more closely the cases observed, and to elucidate whether the mould formation was in a causative relationship to the symptoms of the disease. The decision of this question is, however, very difficult, because *post hoc* is not always the *ergo propter hoc*. I have met with the mould formation particularly in two groups of gastric affections: First, in cases of intense hyperchlorhydria (occasionally attended with hypersecretion and vomiting); and, second, in gastralgia with normal or reduced gastric secretion. It cannot be denied that in many of these cases the mould flakes became smaller in number or disappeared after gastric lavage followed by spraying with a 1 to 2 per mille solution of nitrate of silver. In connection with this a subjective improvement could be observed in the condition of the patient. Yet it cannot be said with certainty that the mould produced the existing pathological process in the stomach, for we find cases analogous in every respect without the presence of mould fungi. Notwithstanding this, it appears plausible that these mould fungi are connected to a certain extent with the above-mentioned abnormal conditions; and even if they are not the cause of these, they undoubtedly increase their severity.

The occurrence of mould in the stomach in large masses must, therefore, be considered of importance from a therapeutic stand-point; hence it must be our endeavor to free the stomach from them as soon as possible. This is best done by irrigation of the stomach in the fasting state of the patient. This acts in a purely mechanical manner, since the mould flakes are removed with the water. The use of the gastric douche might also have a favorable influence in this direction. Following this the application of an antiseptic solution of silver nitrate with a spray appears likewise of some utility. Aside from the therapeutic measures just described the treatment of these cases must be directed in accordance with the special disease present.

**Relation Between Gastric Secretion and Indicanuria.** Jones<sup>1</sup> has examined 162 cases with regard to the condition of gastric juice and also of indicanuria, and found that indican bears no constant relationship to the secretion of hydrochloric acid in the stomach. Strong indican reactions are commonly found in the urine of patients with a copious supply of free hydrochloric acid, and many times indican is absent from the urine of those having not only an absence of free hydrochloric acid in the stomach, but of combined acid also. His observations have been

<sup>1</sup> The Relation of Hydrochloric Acid Secretion to Indicanuria. New York Medical Journal, April 28, 1900.

such that he is not at all warranted in concluding that there is an absence of free hydrochloric acid in the stomach when indican is found in the urine. It cannot be argued that indican will be discovered in the urine of a case in whose gastric contents there is a diminution or an absence of free hydrochloric acid.

In considering the relation of free hydrochloric acid to intestinal putrefaction, according to Jones it is needful to take into account other factors that antagonize putrefactive or fermentative intestinal processes. The degree of combined chlorides and gastric digestion of albuminoids are important in this respect, and observations have confirmed the belief that even in the absence of free hydrochloric acid, provided the nitrogenous constituents of the food are satisfied in the stomach by combination with hydrochloric acid, indicanuria may not infrequently be absent; then there is the probable antiseptic action exerted by the bile as well as that of the pancreatic secretion that must be taken into account. Added to these influences there is perhaps some antiseptic effect exerted by the succus entericus, and it is not improbable that the epithelia lining the intestine may have some inhibiting power over putrefaction. In other words, if the albuminous constituents of the food undergo digestion in the intestine, they do not putrefy, and in many cases indicanuria must be looked upon as an index to the adequacy of intestinal digestion without particular regard to the state of the stomach.

**Condition of the Stomach in Melancholia.** Bell<sup>1</sup> has made extensive examinations with regard to the condition of the stomach (gastric juice, motor function, etc.) in cases of acute melancholia. It was noted that often hyperchlorhydria prevailed.

By a comparison of results in the twelve cases of melancholia investigated by Bell it is interesting and deeply significant to note that in every one of them there is a marked and important departure from the normal. In several cases there was present a total absence of free hydrochloric acid, and in a greater number of cases a great deal too much of it.

In these cases a therapeutic suggestion is plain, namely: To supply hydrochloric acid and pepsin where it is absent or deficient and in the directly opposite condition of hyperchlorhydria, to prescribe an antacid treatment, using the various agents at our command, such as bicarbonate of soda or some of the preparations of magnesia. The problem of the benefit to the patients to be derived from the therapeutic suggestions made in this series of examinations has not yet been properly worked out. However, the results of the medical treatment then established offered some encouragement even after a very short period of trial.

<sup>1</sup> A Series of Analyses in Acute Melancholia of the Stomach Contents after a Test-breakfast. *The Physician and Surgeon*, September, 1899, p. 401.

## THE INTESTINE.

**Auto-intoxication from the Gastro-intestinal Tract.** Jessen,<sup>1</sup> following Pick<sup>2</sup> and McCaskey,<sup>3</sup> ascribes many symptoms, found principally in neurasthenic patients, to auto-intoxication from the intestinal tract. The patients, as a rule, present no objective symptoms whatever. They merely complain of attacks of palpitation—occasionally combined with irregularity of the pulse—of pressure in the head, sudden congestions of the head, followed by a flushed face and dizziness. The patients are without energy and of a somewhat melancholy disposition. In this class of patients Jessen often found Rosenbach's reaction in the urine (burgundy-red color after the addition of nitric acid to the boiled urine), and he believes that this is a proof of the absorption and elimination of toxic products from the intestinal tract.

**TREATMENT.** Jessen treated these patients with high enemas, and had the best results. The symptoms mentioned disappeared, and the Rosenbach reaction could not be discovered in the urine. Beside these water enemas a mixed diet containing but little meat is essential.

**Faulty Assimilation a Cause of Phthisis.** Freund<sup>4</sup> believes that the phthisical habitus so often found in the early youth of people who later become tuberculous is caused by a faulty assimilation in the intestinal canal. Freund found abnormal conditions in the small intestine of tuberculous patients with regard to the digestion of albuminates and carbohydrates, as compared with the normal. While normally, for instance, the total amount of nitrogen in the intestinal contents consists, in its entirety, with the exception of 8 per cent., of albuminates and peptones, the amount of other elements than proteids in the nitrogenous substances of tuberculous patients averages 35 per cent. Again, experiments with the digestion of bread revealed in normal persons the appearance of the entire amount of cellulose in the feces, while in tuberculous patients only 40 to 50 per cent. of this substance could be recovered in the excreta.

**Summer Diarrhœa and Hot Weather.** Chapin<sup>5</sup> shows the great importance of hot weather upon the frequency of intestinal diseases in infants. He gives the following table, which includes the number of deaths from diarrhœal diseases in New York City during the past five years in children under five years of age, through the summer months, with the mean temperature of the corresponding periods :

<sup>1</sup> Ueber cardiale und nervöse Störungen aus gastrointestinaler Ursache. Münch. med. Wochenschr., 1899, No. 43, p. 1409.

<sup>2</sup> Wiener klin. Wochenschr., 1892, Nos. 46 and 47.

<sup>3</sup> Medical Record, September 10, 1898.

<sup>4</sup> Wiener med. Blätter, 1899, No. 42, p. 835.

<sup>5</sup> The Treatment of Summer Diarrhœa in Infants. Medical News, July 15, 1899, p. 65.

|                  | 1894.   |            | 1895.   |            | 1896.   |            | 1897.   |            | 1898.   |            |
|------------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|
|                  | Deaths. | Mean temp. | Deaths. | Mean temp. | Deaths. | Mean temp. | Deaths. | Mean temp. | Deaths. | Mean temp. |
| June . . . . .   | 361     | 70.41°     | 281     | 72.80°     | 363     | 69.80°     | 220     | 67.45°     | 157     | 71.15°     |
| July . . . . .   | 1107    | 74.87      | 1084    | 72.50      | 880     | 76.80      | 914     | 75.92      | 835     | 76.05      |
| August . . . . . | 499     | 70.57      | 648     | 75.60      | 564     | 76.10      | 416     | 73.22      | 650     | 75.83      |
| September . . .  | 346     | 68.81      | 441     | 70.80      | 245     | 67.20      | 319     | 66.99      | 465     | 70.27      |

Having laid down the important hygienic rules of fresh air, frequent baths, cool cloths, and not too frequent feedings, as preventive means of disease, Chapin thoroughly discusses the subject of treating summer diarrhœa.

**TREATMENT.** In the dietetic treatment of summer diarrhœa, bearing in mind that a majority of the cases consist largely of milk-poisoning, all forms of milk must be temporarily withheld. Even the breast may be withdrawn in nursing babies until vomiting ceases. In the interval, water may be frequently given, but in small quantities at a time, if the stomach tends to reject it. The common mistake is in giving too much nourishment at this time, as the infant seems to be weak and in need of support. It is not the food taken but that which is assimilated that supports, hence it is folly to force milk upon a baby at a time when the digestive powers are weakened, if not entirely arrested. Many a summer diarrhœa would be stopped at the very beginning if milk were entirely withheld for from twelve to forty-eight hours. When it is necessary to withhold milk for any length of time, other forms of nourishment may easily be substituted. One of the most easily procurable and satisfactory is egg-water. The white of an egg is thoroughly stirred in half a glass of cool water. This forms a pure and easily assimilable albumin water. The only objection is its tastelessness, and Chapin overcomes this by the addition of about ten drops of aromatic spirits of ammonia. In case there is a tendency to vomit, this aromatic stimulant in small doses, as above, seems to check the stomach irritation. Among other substitutes for milk may be mentioned thin gruels made from barley or wheat flour and cold whey. When the cereals are used the starch may be easily dextrinized by one of the preparations of diastase that are now on the market. If cow's milk is withheld for several days or longer, mutton-broth from which all the fat has been carefully skimmed makes a good substitute. Expressed beef-juice with the fat removed and diluted with cool water makes a stimulating and nourishing drink. When the acute symptoms have subsided and milk is resumed it must be tentatively begun at long intervals and with high dilution.



With regard to drugs, Chapin employs but very few medicaments. He recommends calomel, one-tenth of a grain, every hour, until six or eight have been administered. These small doses act as a sort of stimulant to the bowel, increase glandular secretion, and usually effectively clear the canal of its fermenting contents. The drug is also supposed to have some antifermentative effect. A good-sized dose of castor oil is also effectual, and is followed by a sedative effect on the mucous membrane. If the stomach is very irritable it may be difficult to administer on account of vomiting. Elimination may sometimes be hastened by irrigation of the lower bowel with normal salt solution. Mucus as well as fermenting milk may be thus removed. For those not accustomed to this procedure a hard-rubber rectal tube is preferable, as the soft tube bends on itself on account of the length and marked curve of the sigmoid flexure in infants. The drug that Chapin found most useful in the summer diarrhoea of infants is the subnitrate of bismuth in large doses. A baby of from six to twelve months can take from 10 to 20 grains of the subnitrate every two or three hours. The insoluble quality of the bismuth and its sedative local effect make it most valuable. Irritation and fermentation, even under proper dietetic management, remain longest in the ileum and colon, and this tract is reached by the local action of the bismuth.

Most of the so-called antiseptics have irritating qualities. Chapin does not think that even in antiseptic action they act better than large doses of bismuth. It is manifestly impossible to put the intestinal tract in any condition that can be called antiseptic by the administration of drugs. Small doses of aromatic spirits of ammonia, 10 to 20 drops, well diluted with water, seem to stimulate the mucous membranes and refresh the infant. Alcohol should be given very sparingly in these cases, as it seems to lower the digestive powers. In case of great weakness or collapse, from 10 to 30 drops of whiskey may be administered, well diluted. If the discharges are profuse and exhausting and the baby sinks into a semi-stupor, with depressed fontanelle, very free stimulation with whiskey and ammonia is indicated, as spurious hydrocephalus is thus ushered in. There is one drug that was formerly much abused and is perhaps not used enough now in proper cases, namely, opium. It should never be given combined with other drugs; indeed, diarrhoea mixtures of all kinds are to be depreciated. Opium is contra-indicated until the bowel has been thoroughly emptied of irritating contents, when the stools are scanty and foul-smelling, and when cerebral symptoms threaten. In cases, however, in which rapid peristalsis and profuse glandular secretion persist a few moderate doses of opium are most valuable and may aid in saving life.

**Constipation.** Slagle<sup>1</sup> discusses the subject of constipation in infants and young children. There are infants who are constipated from birth, at least during the first year, and they are usually born of arthritic or nervous parents. This form of constipation is quite rebellious and must be met with baths, massage, dry friction, and afterward with enemas and glycerin suppositories. In infants brought up on the bottle much can be done by the addition of oatmeal-water, cream, sugar-water, and the malt preparations to the milk. In infants, as well as young children, it is of great importance to establish regular habits of stool. This is done by putting the child regularly at the same hour of the day upon the chamber or chair. The palliative means of managing constipation are laxatives, enemas, suppositories, etc. The curative measures consist of diet, habit, massage, etc., carefully managed and persistently employed for several weeks or months.

According to Holt, an average case of chronic constipation in a child, three or four years old, may be managed as follows: Massage for eight minutes morning and evening; the juice of half an orange and a small glass of Vichy immediately on rising; a breakfast of oatmeal with an ounce of cream, dried bread with butter, an egg (soft), half a glass of milk, with cream and water added; a dinner with soup, one starchy vegetable (potato), beefsteak (rare), one green vegetable, baked apple or prunes, dried bread and butter, and only water to drink; a supper of cream-toast, egg (soft), dried bread and butter or graham crackers, half a glass of milk, with cream and water added; this, with an occasional suppository containing nux vomica and hyoscyamus at bedtime, will suffice to complete the treatment.

If the child is puny, dyspeptic, and suffering from malnutrition, tonics and nutrients will be indispensable, among which quinine, iron, and strychnine, or nux vomica, tincture of barks, and the hypophosphites, with extract of malt, cod-liver oil, etc., will be the most efficient.

**The Motor Influence of the Splanchnic Nerve on the Intestine.** Pal,<sup>2</sup> following the experiments of Courtade and Guyon,<sup>3</sup> doubts the correctness of Pflüger's theory of inhibitory nerves of the intestine. He summarizes his conclusions as follows:

1. The splanchnic is a motor nerve of the intestine. It possesses fibres for the innervation of the circulatory muscles as well as of the longitudinal muscles of the intestine.

2. The splanchnic produces inhibitory symptoms by its motor action

<sup>1</sup> Constipation in Infants and Young Children. *Northwestern Lancet*, September 1, 1899, p. 324.

<sup>2</sup> Ueber den motorischen Einfluss des Splanchnicus auf dem Dünndarm. *Archiv f. Verdauungskrankheiten*, Bd v., Heft 3, p. 303.

<sup>3</sup> *Arch. de Physiologie*, 1897.

and regulates by means of the latter the intestinal tone. It is, therefore, unnecessary to assume specific nerves, either for the inhibition or for the tone of the intestine.

3. The appearance of inhibitory phenomena is caused by an analogous and simultaneous action of one and the same muscular layer over a large central portion of the bowel. This phenomenon can be produced by the central apparatus as well as by the splanchnic.

**Perforating Duodenal Ulcer.** Weir<sup>1</sup> reports a case of perforating duodenal ulcer, with operation. He gives the following points as aiding in the diagnosis of this affection :

Great pain is usually felt at the epigastrium or to the right of this region. In twenty-three of forty-seven instances it was simply recorded as abdominal pain. Vomiting often follows the attack of pain. It occurred in twenty-eight out of thirty-four instances. Shock is not often met with, but may be severe and fatal. Peritoneal symptoms rapidly develop, with a tendency in some cases to be localized in the upper part of the abdominal cavity and in the right side ; when these signs show themselves mostly to the right and at or below the level of the umbilicus the picture necessarily simulates an appendicitis. When the liver dulness has been dissipated up nearly to the mammary line, air extravasation may be suspected, and when accepted as present it will aid in concentrating the diagnosis. The symptom of liver resonance, unless marked, is so often found to be due to a distended colon that it should not be much relied on.

In considering the diagnosis of a perforated duodenal ulcer as just given, according to Weir more weight and attention should be given first to the previous history, which shows, contrary to the opinions of many previous observers, that in the fifty-one collected cases of operations for the relief of such conditions there was a history of gastric or dyspeptic symptoms given in twenty-five out of thirty-four instances, where this point was noted ; secondly, and also important, is the fact that the initial or early pain was developed in twenty-six instances out of forty-seven in the epigastrium ; and in the right hypochondrium thirteen times. The third factor of value in the diagnosis, as well as the treatment of the symptoms of perforation peritonitis, whether from stomach, duodenum, gall-bladder, appendix, or any other part of the intestinal tract, is the early resort to an exploratory incision. This need of an early solution of the site of a perforation has been clearly shown in cases of gastric perforation in an article by Weir and Foote,<sup>2</sup> embracing seventy-eight cases operated on for this trouble. The mortality clearly

<sup>1</sup> Perforating Duodenal Ulcers. *Medical News*, May 5, 1900.

<sup>2</sup> *Medical News*, April 25, 1896.

depended on whether the patient underwent surgical intervention within twenty-four hours from the inception—*i. e.*, the pain—of the perforation.

**Appendicitis.** Richardson<sup>1</sup> is of the opinion that the appendix should be removed if the diagnosis of appendicitis is made in the first hours of the attack. After the early hours he advises operation :

1. If the symptoms are severe, and especially if they are increasing in severity.

2. If the symptoms, after a marked improvement, recur.

3. If the symptoms, though moderate, do not improve.

The wisdom of the operation is questionable :

1. In severe cases in which an extensive peritonitis is successfully localized and the patient is improving.

2. In cases which are at a critical stage and which cannot successfully undergo the slightest shock.

Richardson discusses also the question whether the appendix should be removed in every case. It should be removed :

1. In localized abscesses with firm walls.

2. When the patient's strength does not permit prolonged search.

It should be removed whenever the peritoneal cavity is opened, unless the patient's condition forbids.

The appendix should be removed in all cases as soon as the inflammatory process has had time completely to subside—in from two to three months after the attack. In cases simply drained the scar tissue should be excised, the appendix removed, and the wound securely sutured.

**TREATMENT OF APPENDICITIS.** Love<sup>2</sup> advises treating appendicitis with rectal injections, cold or warm poultices, starvation diet, and absolute rest ; he is absolutely against the use of opiates. Love is in favor of appendectomy, even during the first attack, provided a good surgeon is at hand ; otherwise he prefers the outlined medical treatment.

**Dilatation of the Colon.** F. T. Stewart and Hand<sup>3</sup> report a case of undoubted congenital dilatation of the colon in a boy, aged six years. At the autopsy the following condition of the abdomen was found : the spleen, liver, small intestines, and urinary apparatus presented nothing unusual. The colon was so large that instead of framing the small intestines it almost completely hid them from view, and after being slit longitudinally and spread out on the table measured transversely 17 cm.—*i. e.*, the circumference was 17 cm. when not distended. Ten cm.

<sup>1</sup> Appendicitis. American Journal of the Medical Sciences, December, 1899.

<sup>2</sup> Appendicitis from a Medical Stand-point. Journal of the American Medical Association, January 6, 1900.

<sup>3</sup> Dilatation of the Colon. Archives of Pediatrics, March, 1900, p. 161.

above the ileocæcal valve was a hard, fibrous constriction, 6 cm. in circumference; 30 cm. above the anus a similar constriction, 5 cm. in circumference, and between the constrictions numerous large, transverse, superficial ulcerations measuring from 3 to 5 cm. in their longest diameter. The colic walls were hard, thickened, and corrugated, resembling tripe. The rectum measured 16 cm. in circumference.

Idiopathic dilatation of the colon is not always congenital, and may occur in any decade of life. Whenever it appears it is progressive and malignant. Medical treatment affords but little help, while some cases have been treated surgically with gratifying results. One is confronted with a large fecal reservoir whose walls are frequently lined with ulcers and from which septic material is constantly being absorbed.

The operative procedure best suited for this condition could be definitely outlined at the time of operation only, the objective point being either drainage or removal of the large bowel. If the patient be *in extremis* an artificial anus would be indicated, leaving more radical measures to a later period. If undertaken with the patient in good condition, a resection of the sigmoid might be advisable, as great distention of this portion of the large bowel alone has been observed in several cases; or the ileum might be implanted into the rectum and the lower end of the colon sutured in the abdominal wound so as to drain it, thus sidetracking the entire large bowel and leaving it to atrophy.

It seems that all cases of chronic constipation with a persistently swollen abdomen should be scrutinized by the surgeon. Often in the congenital form the post-mortem examination only will demonstrate whether the dilatation be idiopathic or due to a narrowing of the lower bowel or other definite cause. Often in the acquired class it will be impossible to surely differentiate an idiopathic case from one due to partial volvulus or other equally remediable condition; and although the surgeon finds no obvious cause, he may yet adopt a course shaped to save life, mitigate suffering, or cure the patient.

**Amœbic Dysentery.** Diamond<sup>1</sup> reports five well-observed cases of amœbic dysentery, and one with fatal issue in which an autopsy was made. The changes here observed were largely confined to the mucosa and muscularis mucosæ, any deeper ulceration being apparently secondary. The earliest changes show that the mucosa at the point which forms the beginning of the ulcer has become transformed into a peculiar homogeneous granular mass, which gradually softens and breaks down at the surface; while the mucosa near the seat of the degeneration is seen infiltrated with small round-cells, which may even extend through

<sup>1</sup> Amœbic Dysentery. Philadelphia Medical Journal, April 7, 1900, p. 817.

the muscularis into the submucosa. The bloodvessels are dilated and filled with blood. Amœbas are occasionally seen near the surface of the mucosa, but usually they are deeper, and especially along the margin of the muscularis. This layer also shows marked changes. The nuclei have disappeared and the fibres at the seat of the ulceration are granular. Beyond this point it seems that the muscularis has undergone a kind of hyaline transformation. Many amœbas are seen in this layer, lying between the fibres, which are swollen and separated from each other. In these sections the ulceration rarely extends any deeper than the submucosa. In the submucosa there is a decided increase of fibrous tissue.

Diamond advises staining the sections in a dye produced by mixing toluidin-blue and carbol-fuchsin. The amœbas stain a purplish-blue color, the nuclei of cells either blue, purplish-blue, or red, and the rest of the tissues light to purple-red. The sections should remain in the stain from ten minutes to several hours; they are then washed in alcohol and cleared in xylol. The internal structures of the amœbas are beautifully shown when the washing with the alcohol is a little prolonged. The vacuoles become quite distinct, and apparently surround small granules, reddish or pinkish in color. If the toluidin-blue is in excess the tissues and the amœbas are then stained more of a blue. This stain keeps well and does not deteriorate. It is made as follows: Toluidin-blue, saturated aqueous solution 1 part; carbol-fuchsin (tubercle stain), 1 part; mix; filter. This combination acts quickly, bears washing, is delicate, and gives the effect of a double stain. A somewhat similar result is obtained when the tissues are stained in carbolic acid and toluidin-blue and counter-stained with eosin.

**TREATMENT.** As the best treatment for this disease Diamond considers rectal injections of solutions of hydrogen dioxide and potassium permanganate. Of the former a 25 per cent. solution can be used, and of the latter 15 grains to the quart of warm water, to be injected two or three times a day and gradually reduced according to results. Out of twenty-five cases treated with hydrogen dioxide by Harris eight were cured and four greatly benefited. Three of Diamond's comparatively acute cases completely recovered, two of which were treated with potassium permanganate and the other with hydrogen dioxide. A good quality of this agent was not at the time at hand, therefore the potassium permanganate was used, and with good results. While marvellous results are sometimes obtained with hydrogen dioxide, a guarded prognosis must be given, as relapses are frequent, especially in chronic cases. A patient should not be considered out of danger for at least two months after apparent recovery. During that period the patient should remain on a liquid diet.

**Ankylostomiasis.** Ashford<sup>1</sup> draws attention to the prevalence of ankylostomiasis in Puerto Rico. Among twenty cases of severe anæmia he has examined, he found the eggs of ankylostoma in nineteen. It is easily conceivable why in these cases the usual remedies for anæmia had been given without any benefit. Soon after the recognition of the etiological factor of the anæmia in these cases, Ashford treated them successfully by purgatives and vermifuge remedies. Thymol and male fern seemed to act best. The bad hygienic conditions of the island and the poor diet must be made responsible for the prevalence of this disease in Puerto Rico.

## THE LYMPHATICS.

**Obliteration of the Receptaculum Chyli.** The diagnosis of obstruction of the thoracic duct has been made only in a few cases. In almost all of them there was present a cancerous disease of the abdominal viscera, accompanied by ascites, the latter on tapping showing a chylous fluid. It is this character of the fluid which made the recognition of the obstruction of the duct probable. This refers to the cases recorded by Schramm,<sup>2</sup> Hektoen,<sup>3</sup> Senator,<sup>4</sup> and Leydhecker.<sup>5</sup> Smith<sup>6</sup> has observed two cases of obliteration of the duct, and believes it possible to recognize this condition, even when there is no chylous ascites present, principally by the extremely rapid emaciation encountered.

Smith says: "It would seem that when with symptoms of disease in or about the stomach we have more rapid emaciation than can be otherwise explained, we are justified in making the diagnosis of probable obliteration of the receptaculum chyli, and that this probability will be increased to a very strong presumption if there are in addition rather copious, pale, semi-fluid passages from the bowels. Under such conditions we should not place much dependence upon fatty substances as articles of diet. Milk, so much relied upon in gastric disorders, will be useful only for the proteids and the sugar which it contains. Albuminous and saccharine or sugar-producing foods must be employed in sufficient quantity to compensate for the loss of the fats."

<sup>1</sup> Ankylostomiasis in Puerto Rico. *New York Medical Journal*, April 14, 1900, p. 552.

<sup>2</sup> *Berl. klin. Wochenschr.*, 1896, p. 955.

<sup>3</sup> *Arch. f. pathol. Anat.*, 1894, p. 357.

<sup>4</sup> *Charité-Anal.*, 1895, p. 203.

<sup>5</sup> *Arch. f. pathol. Anat.*, 1893, p. 135.

<sup>6</sup> Can We Diagnosticate Obliteration of the Receptaculum Chyli? *Medical Record*, December 2, 1899, p. 813.

## THE PANCREAS.

**Pancreatic Digestion.** Rachford<sup>1</sup> has made extensive studies with regard to pancreatic digestion and also with reference to the anatomical position of the pancreas, gall-bladder, and the duodenum in different animals. In some of the herbivorous animals he found the gall-bladder absent, while it was present in all carnivorous animals. Rachford, therefore, concludes that the absence of the gall-bladder in these herbivorous animals clearly indicates the unimportance of this organ in starch digestion. The presence of a gall-bladder in all carnivorous animals indicates that there is a physiological necessity for a reservoir of this kind for holding the bile so that it can be discharged in quantity into the duodenum during the pancreatic digestion of fats and proteids. That this reservoir for bile is unnecessary in herbivorous or starch-eating animals is clearly proven by the fact that it gradually diminishes in size as the animal takes less fat and proteid in its food, until in some of the exclusively herbivorous animals it is absent. Clearly, then, the character of the food in different species of animals determines the presence and size of the gall-bladder. In the carnivora the gall-bladder is large, and in the herbivora it is small or altogether absent, while in the omnivora it is intermediate in size. The physiological inference from these facts is that bile does not serve any very important purpose in the pancreatic digestion of starches.

Rachford also calls attention to the following important facts in the comparative anatomy of the small intestine: The duodenum in the carnivora is more closely attached to the head of a fleshy pancreas and has a shorter mesenteric attachment than it has in the herbivora. These facts make peristaltic and other movements less active in the duodenum of the carnivora than in the herbivora, and, therefore, cause the food to remain longer in the duodenum of the carnivora than in the herbivora. The horseshoe shape of the duodenum in the carnivora may also contribute to this same end. It appears, therefore, that certain anatomical conditions have been developed in the carnivora which have the effect of so slowing the rate of passage of food through the duodenum that the time of exposure of foodstuff in the duodenum of these animals to the action of bile and pancreatic juice is greater than in the herbivora.

From these facts one would infer that it is of physiological importance that the fats and proteids should be retarded in their passage through the duodenum in order that they may be longer acted upon by the bile and pancreatic juice while the food yet contains combined acid and

<sup>1</sup> Pancreatic Digestion from the Stand-point of the Comparative Anatomy of the Bile and Pancreatic Ducts in Mammals. *Medicine*, May, 1900, p. 380.



before it reaches the alkaline succus entericus of the jejunum and ileum.

**Pancreatitis.** Carmalt<sup>1</sup> has observed two cases of pancreatitis with fat necrosis. In both these were symptoms indicative of intestinal obstruction or advanced appendicular disease; yet, when subjected to a laparotomy, neither of the latter lesions was found, but fat necrosis of the omentum and mesentery in consequence of pancreatitis. Pancreatitis is met in an acute, a hemorrhagic, and a suppurative or gangrenous form. The fat necrosis accompanying the different forms of pancreatitis seems to be due, according to Flexner,<sup>2</sup> to the presence of the fat-splitting ferment (escaping from the pancreas) in the diseased foci.

THE SYMPTOMATOLOGY of this disease has been greatly advanced by Fitz,<sup>3</sup> Stockton,<sup>4</sup> Flexner, Williams<sup>5</sup> and others. In most cases described in the literature there was a history of repeated attacks or of a habit of indigestion. The patients were frequently alcoholics or plethoric and corpulent and prone to overeating. Gallstones have often been found present in these cases.

The attack which culminates in the disease under consideration is often one of several, not differing in its inception from others already recovered from, except in its severity and persistence. This is particularly the case with alcoholics, who are exceedingly fond of calling themselves "bilious" (whatever that may mean), and taking their blue mass to get straightened out from their indiscretion.

The general initial symptoms are vomiting and abdominal pain of a colicky character, *referable principally to the epigastrium*; there is prostration and anxiety; flatulence with moderate tympanites; after a short time general abdominal tenderness becomes prominent, usually without localization, though sometimes the epigastric region is especially sensitive; nor is there induration such as we find in appendicitis, with which the disease is often confounded. The movement of the bowels may, in the beginning, be either frequent or constipated, but the latter condition so frequently develops later, and is so difficult to overcome that an intestinal obstruction is suspected and the attempt made to relieve this by operation. In other cases the abdominal pain localizes itself in the epigastric region in general, and a tumor develops, deeply seated at first, approaching the surface later, and an exploratory operation reveals the true state of affairs.

<sup>1</sup> A Contribution to the Relation of Pancreatitis to Abdominal Surgery. Yale Medical Journal, November, 1899, p. 15.

<sup>2</sup> Journal of Experimental Medicine, 1897, vol. ii., p. 413.

<sup>3</sup> Boston Med. and Surg. Journal, December 19, 1899.

<sup>4</sup> American Journal of the Medical Sciences, September, 1895.

<sup>5</sup> Journal of Experimental Medicine, November, 1898.

**DIAGNOSIS.** According to Carmalt, the diagnosis of suppurative pancreatitis has been made only twice before the laparotomy. Several cases of hemorrhagic pancreatitis have been subjected to operation without positive diagnosis, but, with one exception, unsuccessfully. The clinical indications for operative intervention are uncertain. In general, cases of hemorrhagic pancreatitis are of much greater severity than those of the suppurative form. The pain and tenderness in the epigastrium and umbilicus are greater; the nausea and vomiting more violent; the collapse approaches to fainting; the pulse is exceedingly weak and fluctuating. The temperature is not markedly elevated; indeed, it has been noted to be subnormal in several cases. The distention and tympanites are marked—in the beginning in the upper part of the abdomen; later, as the constipation, which is usually present, increases, the whole abdomen is distended. Sometimes there is albumin in the urine, at others there is sugar. Jaundice has been mentioned twice. The course of the disease is rapid, lasting but a few days. In a large proportion of the cases intestinal obstruction is regarded as the condition—in others the diagnosis of perforation of the stomach is made. Gastro-duodenitis and poisoning are also mentioned as explaining the condition. Diagnosis of this condition is but seldom made. Fitz made it in one case.

Körte<sup>1</sup> regards these cases as beyond diagnosis, owing to their rapid course; but advises measures looking to prolonging life, hoping to keep them alive until a gangrenous or suppurative pancreatitis gives a chance for operative interference. With this object in view he suggests irrigation of the stomach, nutritive and stimulating enemata, intravenous injection of normal salt solution, etc.

The diagnosis of the gangrenous state is made by finding, after the symptoms just detailed have lasted some days, a swelling in the position of the pancreas with the constitutional evidences of suppuration. Such a condition being detected, Körte advises a laparotomy with as little delay as possible.

In some instances the pancreas was found sequestered and floating in an abscess. Still, such a condition must not necessarily be entirely unfavorable for an operation. One might well hesitate to undertake the elimination from the economy, in whole or in large part, of an organ so large as the pancreas, were it not that the organ, as such, has long ceased its function, and there is on record a case where the entire pancreas was passed per rectum after an attack of this kind, and the patient lived for seventeen years afterward.

In a few cases diabetes has been a complication, influencing unfavorably both the immediate recovery and subsequent course; but when one

<sup>1</sup> *Verhandlungen der Deutschen Gesellsch. f. Chirurgie*, 1894, i., p. 157; ii., p. 365.

considers the sugar-producing function of the organ it is rather surprising that it plays so unimportant a rôle.

**Pancreatic Hemorrhage.** Anders<sup>1</sup> reports two cases of his own, with pancreatic hemorrhage and death. In one he made the diagnosis during life. He also gives a tabulated list of forty cases of pancreatic hemorrhage found in the literature.

Among predisposing factors are sex and age—males, after the middle period of life—and the alcoholic habit. He was able to collect forty cases of pancreatic hemorrhage. Of the 40 cases 25 were males and 9 females, while in the remainder the sex was not given. The ages of 30 of the patients was stated; they ranged from twenty-six to seventy years; and 13 of the 30, or about 43.3 per cent., occurred in patients over forty-five years of age. Of the remaining 17 cases 3 were twenty-eight years of age, 2 were aged thirty years, and 3 the age of thirty-one years, while the youngest was only twenty-six years of age. There was a history of chronic alcoholism in 12 cases, or about 30 per cent; but since special reference to this habit is made in only 18 cases, the percentage is much higher, or about 66.6 per cent. It is currently stated that a rich diet also engenders predisposition to pancreatic apoplexy, presumably by impairing the histological integrity of the vascular walls, especially in an atheromatous subject.

From Anders' personal experience and an examination of the literature the belief is well founded that pancreatic hemorrhage, particularly as an immediate cause of death, is of greater clinical and medico-legal importance than has hitherto been supposed. It must be confessed, however, that the condition is comparatively infrequent, although not by any means a curio among clinical and pathological findings. According to Draper, who met with 19 cases of pancreatic hemorrhage in 4000 autopsies, the condition is rare; in 9 or 10 of this series it was the sole discoverable cause of death. Cases are also recorded in which persons had been found dead or died from extensive hemorrhagic extravasations in the pancreas or surrounding tissues or cavities before medical aid could be summoned. On the other hand, the immediate effects of the bleeding may be survived, and death occur at a later period in consequence of shock and increasing anæmia.

## THE LIVER AND GALL-BLADDER.

**Floating Liver and its Clinical Significance.** The occurrence of floating liver was first noted upon the dissecting-table by Sauvage,<sup>2</sup> later

<sup>1</sup> Pancreatic Hemorrhage. *Journal of the American Medical Association*, December 2, 1899, p. 1391.

<sup>2</sup> *Nosol. method. sistens morborum classis*. Amstelod., 1768, t. i., p. 208.

by Portal,<sup>1</sup> and subsequently demonstrated clinically on living subjects. Cantani<sup>2</sup> was the first to describe a case of floating liver in a woman in 1866. He was followed by other authors, who reported isolated cases of this affection, as, for instance, Piatelli,<sup>3</sup> Meissner,<sup>4</sup> Winkler,<sup>5</sup> Sutugin,<sup>6</sup> Chvostek,<sup>7</sup> Wassiliew,<sup>8</sup> E. Smith,<sup>9</sup> Kisbert,<sup>10</sup> Landau,<sup>11</sup> Graham<sup>12</sup> and others. In 1889, I reported<sup>13</sup> a case of floating liver in a man, published in the *New Yorker medicinische Monatschrift*. In a recent number of the *Medical Record*<sup>14</sup> I again discussed this subject, not because I consider floating liver as of rare occurrence, but rather for the reason that I am convinced of its relative frequency; and, further, since, when overlooked, it may often give rise to diagnostic errors.

**DEFINITION.** By the term floating liver (movable liver, *hepar migrans*, *ectopia* or *luxatio hepatis*, *hepatoptosis*) we designate in general a liver which has fallen downward and can usually be restored to its normal position, partially or completely, by certain manipulations.

**ETIOLOGY.** The etiology of floating liver has not as yet been entirely elucidated. As in the case of floating kidney, the corset has here also been held responsible, especially by Cruveilhier. It must indeed be conceded that the tight lacing with this modern apparel may exert a detrimental influence upon the position of the abdominal organs; yet floating liver occurs in persons who have never worn a corset. Frequent pregnancies, which often produce pendulous abdomen, have been regarded by Cantani and Winkler as a cause of this condition. This fact, however, although certainly very significant, cannot operate in all cases, for floating liver is also found in virgins and males.

According to Landau, the factors which are chiefly to be held responsible for the occurrence of floating liver are: (1) Lacerations of the

<sup>1</sup> Cours d'Anatomie médicale. Paris, 1804, t. v., p. 323.

<sup>2</sup> Caso di fegato ambulante. *Annal. univers di Medicina*, Milano, November, 1865, pp. 373-383.

<sup>3</sup> Fegato ambulante. *Revist. clin.*, 1868, vii., p. 239.

<sup>4</sup> Die wandernde Leber in ihren correlativen Beziehungen zur Schwangerschaft, Geburt und Wochenbett. *Schmidt's Jahrb.*, 1869, Bd. cxli., p. 107.

<sup>5</sup> Zur Casuistik und Aetiologie der Wanderleber. *Arch. f. Gynäkolog.*, 1872, Bd. iv., p. 104.

<sup>6</sup> Zur Casuistik der Wanderleber. *Arch. f. Gynäk.*, 1875, Bd. viii., p. 531.

<sup>7</sup> Ein Fall einer wandernden Leber. *Wiener med. Presse*, 1876, Nos. 29, 30.

<sup>8</sup> Ectopia hepatis et lienis. *St. Petersburg. med. Wochenschr.*, 1876, No. 30.

<sup>9</sup> Movable Tumor in the Abdomen, Simulating Movable Kidney; Necropsy, Displacement of Liver. *Lancet*, April 1, 1883.

<sup>10</sup> Ein Fall von Wanderleber. *Berl. klin. Wochenschr.*, 1886, No. 24.

<sup>11</sup> Die Wanderleber und der Hängebauch der Frauen. Berlin, 1885.

<sup>12</sup> Displacement of the Liver. *Transactions of the Association of American Physicians*. Philadelphia, 1895, p. 258.

<sup>13</sup> Ein Fall von Wanderleber. *New Yorker medic. Monatschr.*, July, 1889.

<sup>14</sup> Floating Liver and its Clinical Significance. *Medical Record*, September 16, 1899.

ligamentous structures of the liver (ligamentum coronarium, ligamenta triangularia, and the other peritoneal bands), which may originate through an acute trauma, and much more frequently through repeated ones. (2) An enlargement of the capacity of the abdominal cavity followed by the dislocation of the abdominal and pelvic organs and indirectly of the liver; for the latter, normally, through the girdle-form support of the abdominal walls, is carried upon the intestines like a cushion; if the intestines slip down a descent of the liver will then readily take place. Lacerations of the ligaments can occur either through a sudden trauma, such as lifting heavy burdens, falls, etc., or—and this occurs much more frequently—through repeated traumas; among these must be placed sudden and forcible expirations, as in cough, sneezing, and paroxysms of laughing. I have observed a case of suddenly appearing floating liver in a man, aged forty-three years, after lifting a burden of 300 pounds. On the following day the patient suffered from slight somnolence and icterus. On examination I found the liver as a prominent tumor beneath the ensiform process, while the area of hepatic dulness on the right half of the thorax was almost entirely absent.

As regards the significance of frequent forcible expirations, I observed a case of floating liver in a singer, and am positively of the opinion that the laborious work of the diaphragm incident to this vocation may lead to giving away of the hepatic ligaments.

The enlargement of the abdominal cavity may result from rapidly progressive emaciation (disappearance of the adipose layer of the omentum, kidneys, etc.), through which more space is left free in the abdominal cavity, or after childbirths and removal of abdominal tumors. That this factor is of great significance in the occurrence of floating liver as well as ptosis of the other abdominal organs is beyond doubt. In most instances, however, this condition *per se* is not sufficient to produce floating liver; ordinarily other predisposing factors must co-operate in the development of this affection.

As regards the frequency of floating liver, Landau stated that he regarded this condition as quite common. In 1887, Glénard observed in 1300 patients 51 cases of hepatoptosis, among which 32 were complicated with movable kidney; 30 occurring in women and 2 in men.

In the last ten years, since I have given the subject of dislocation of the liver my attention, I have frequently noted this anomaly; but as I did not accurately examine every patient with reference to this point, the total number of cases observed by me is too small in order to compute the frequency. I, therefore, only make use of material which I have had occasion to observe in the last five months of the year 1899 (January to May). All these patients were accurately examined as to

the position of the liver, as well as of the other abdominal organs, and, therefore, the acquired figures must be approximately correct. During the period referred to above I have seen in my private practice 804 patients (particularly subjects of gastro-intestinal diseases). Among these there were 435 men and 369 women. Of these 804 patients 30 were cases of floating liver; 21 women, 9 men. Expressed in percentages, the total number of those affected with floating liver would be 3.7 per cent. of all persons suffering from digestive disorders. If we compute the relative frequency of floating liver separately for both sexes we obtain 5.6 per cent. for the female and 2 per cent. for the male sex. Among 21 women with floating liver 10 also had floating kidney, which was bilateral in 3 cases. There was no sign of pendulous abdomen in 5 of the women, while the remaining 16 had a moderate degree of abdominal flaccidity.

**SYMPTOMATOLOGY.** Cases of floating liver can be divided into the following five groups:

1. Cases unaccompanied by symptoms, in which the floating liver gives rise to no disturbances.

2. Dyspeptic cases, with indefinite digestive disturbances in conjunction with a feeling of weakness and certain other nervous symptoms.

3. Cases of hepatalgia, in which almost constantly pains are present on the right side of the abdomen (hepatic region), which often radiate toward the back and shoulder-blades. These pains frequently subside in the recumbent posture. In many instances sensations of a drawing and tearing character are present.

4. Cases of hepatic colic in which colicky attacks occur similar to gallstone colics. In these no icterus is commonly present, although it may appear in rare instances.

5. Asthmatic cases, in which a feeling of fulness and constriction in the upper abdominal region, associated with slight dyspnoea, is especially prominent.

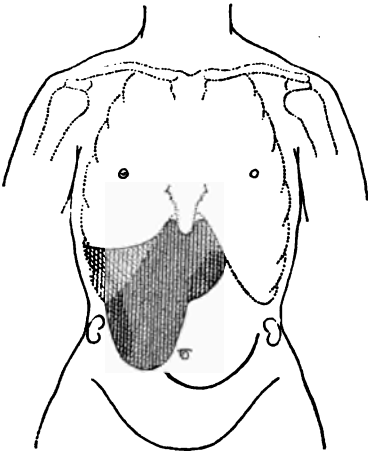
I have often had occasion to observe floating liver without any special symptoms, and such cases are also cited in the literature.

In my article typical cases of all the different four groups, with symptoms, have been described. Here I do not consider it amiss to insert the drawings,<sup>1</sup> showing the position of the liver in my cases described in the *Medical Record*. (See Figs. 13 to 21.)

<sup>1</sup> In all the annexed figures the intensely dark places mark the configuration of the liver accessible to palpation; the slightly darkened, the area of dulness on percussion of the organ. The line drawn below the navel on the left side of the abdomen shows the outline of the greater curvature of the stomach. The kidneys are stretched only if accessible to palpation.

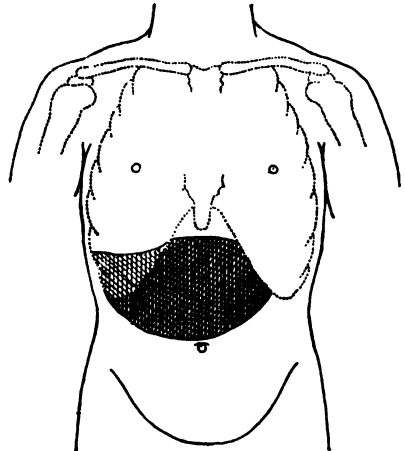
**DIAGNOSIS.** The diagnosis of floating liver is based upon the demonstration of the fact that this organ has left its normal limits above in the thorax and has been displaced more or less forward and downward. Percussion will show that the upper boundary of the area of liver dulness in the thorax is no longer situated at its normal place, but has been

FIG. 13.



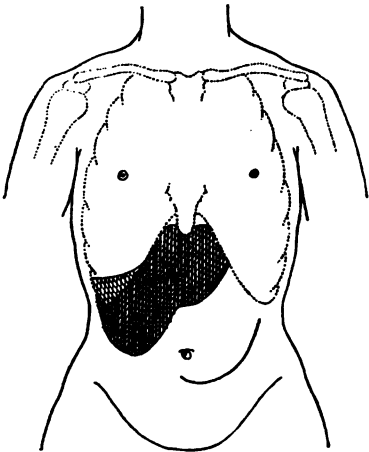
Mrs. Sarah D.

FIG. 14.



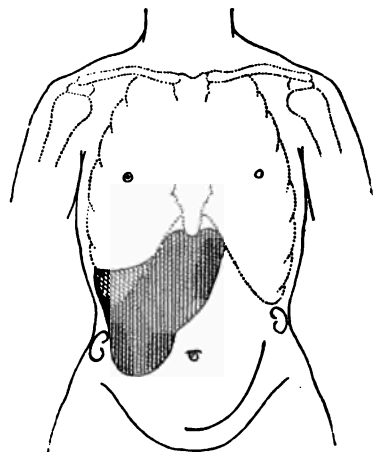
Abraham G.

FIG. 15.



Mrs. N. Z.

FIG. 16.



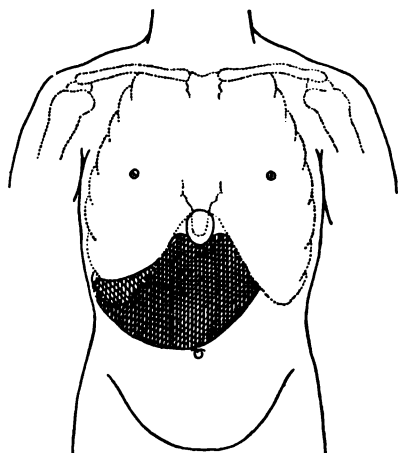
Mrs. E. A. S.

shifted downward. While normally the area of liver dulness begins in the right mammary line at the fifth intercostal space, it is now to be detected at the level of the seventh rib or at the border of the ribs. Corresponding with this, the zone of dulness at the back of the thorax is also placed more deeply. Occasionally a tympanitic sound is detected

over the ensiform process, and this is of special importance, since it shows that the intestines or stomach lie above the left lobe of the liver.

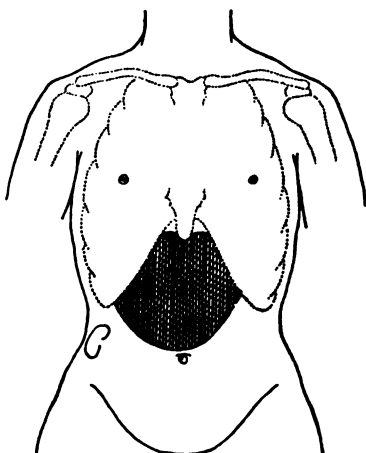
Downward from the right margin of the ribs, in the mammary line and extending toward the right from this point, where normally liver dulness terminates, there is found an area of dulness extending down-

FIG. 17.



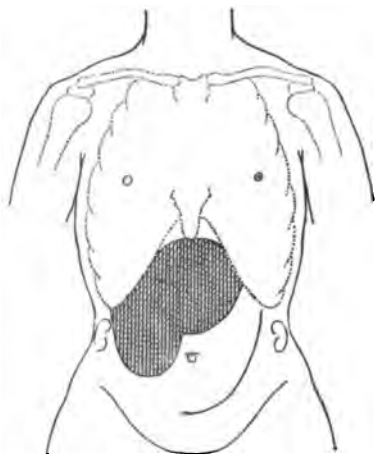
David L.

FIG. 18.



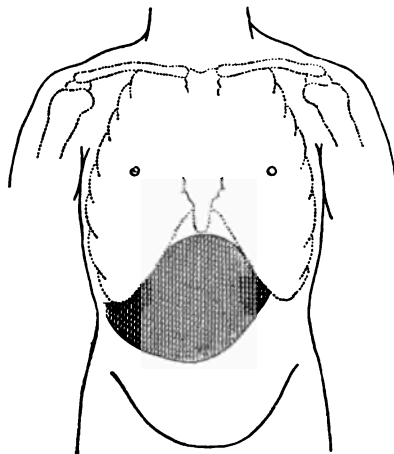
Mrs. Minna F.

FIG. 19.



Mrs. L. M. R.

FIG. 20.



Abraham S.

ward to the navel or even to within a few centimetres above the symphysis. In order to determine exactly the upper line of dulness we may percuss from the border of the ribs downward until we meet the tympanitic intestinal resonance; or, better still, we may practice percussion from below upward—that is, commencing in the lowermost abdominal region and proceeding in a straight line upward until we



discover the dull sound of the liver. It should be remarked, in this connection, that percussion is to be carried out quite delicately, since through forcible tapping the tympanitic resonance of the intestines subjacent to the liver becomes perceptible, and the object of percussion is thus marred.

In the examination of floating liver palpation is of the greatest significance; as in the case of floating kidney, it is the most valuable method of examination. By means of palpation alone it is possible in many cases to make a diagnosis of floating liver, although sometimes it must be further elucidated through percussion.

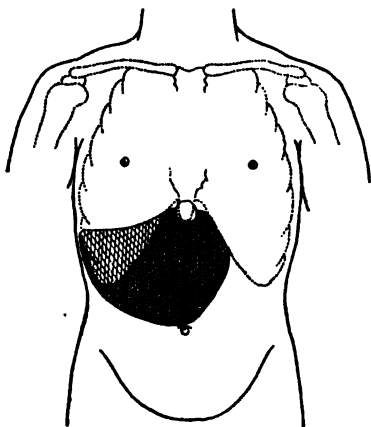
Palpation is here best carried out without the exertion of strong pressure and by means of the palmar surface of the fingers and often of the entire hand. It is most advantageous to commence the examination closely below the right border of the ribs, and, palpating slowly, to proceed from here in a downward direction. In cases of floating liver we are always able to find a portion of the liver surface at this place; usually the liver can then be traced downward as far as the navel, or still further below this point, in the form of a tumor with a smooth surface. Often at the lower margin of resistance the lower liver border, with its incisure, can be accurately palpated. Occasionally, by passing the fingers somewhat further up between the lower border of the ribs and the liver, it is possible to discover the convex surface of the liver. In marked cases of ptosis of the liver nearly the entire organ can be palpated both above and below, and the right as well as the left hepatic lobe mapped out exactly.

Palpation as well as percussion should be carried out both in the recumbent and upright posture, because in cases of highly developed mobility of the liver the organ sometimes shifts back spontaneously more or less to its normal position when the patient lies down.

Inspection shows in some cases a prominence either of the entire upper abdominal region or a slight protuberance of the abdomen upon the right side. Inspection often contributes toward awakening a suspicion of floating liver, but is never sufficient alone to establish the diagnosis.

The condition of mobility of the liver is investigated in a recumbent posture of the patient. After having practised palpation we attempt by means of pressure upon the abdominal walls with one hand, or, in case of large size of the liver, with both hands, to move the organ in a

FIG. 21.



Mrs. K.

direction from below and behind, upward and forward. If a complete or partial reposition is possible, and the liver is retained in its new position by an assistant or by the patient himself, the line of dulness at the right side of the chest is found to have been shifted upward. As a matter of fact, reposition cannot be carried out in all cases of floating liver. Occasionally the mobility of the organ from the right toward the left, and *vice versa* from the left to the right, can be demonstrated, while its displacement upward meets with difficulties, especially in patients with tense abdominal walls.

**DIFFERENTIAL DIAGNOSIS.** To make a positive diagnosis of genuine floating liver it is not sufficient to determine that the organ has left its normal position, but it must also be shown that no diseases of the intrathoracic organs have caused a filling up of the thoracic cavity, and thus have given rise to a downward displacement of the liver. This is, of course, very easy, since such processes (pleuritic exudations, subphrenic abscess, etc.), if developed in a high degree, can be recognized without difficulty. On the other hand, if not marked they do not lead to descent of the liver.

Enlargement of the liver or hepatic tumors, aside from their peculiar shape, are in general recognized by the fact that the liver is to be found in its normal position (as shown by percussion of the thorax) and that these tumors directly merge into the organ. Errors in the diagnosis of floating liver in cases in which other tumors are present have often been made.

These mistakes will, however, rarely or never occur with thorough methods of examination. A constricted liver will scarcely ever be mistaken for floating liver, since in the former the liver is situated in its normal place, and only part of it is found further downward.

**TREATMENT.** The treatment of floating liver resembles, on the whole, that of enteroptosis, and especially that of floating kidney. Here, also, the chief measure is the application of well-fitting abdominal bandages, which support the lower half of the abdomen in an upward direction and increase the tension of the abdominal walls. A special pad for pressing the liver still further back is of as little service here as in floating kidney. Aside from this, so to speak, orthopedic treatment of the abdomen and other physical and dietetic means must be considered. General massage and hydrotherapeutic measures which have for their aim the strengthening of the organism are of high value. In the front rank of all these methods is an appropriate diet. In most weakly individuals an abundant diet (or, rather, forced feeding) must be prescribed. The patient should be directed to take as much food as other healthy persons, and a little more. If, beside the ordinary diet, an additional quarter of a pound of butter is ordered daily, much will be accomplished by this means alone, and most of the patients will

soon show an increase in weight. On the other hand, persons who are heavy eaters and rather inclined to corpulency should reduce the amount of food within proper limits.

Gymnastic exercises in the open air, and, in cases with a tendency to constipation, special exercises for the abdominal muscles, are, likewise, of value. Occasionally, particularly when the gastric and intestinal symptoms are strongly pronounced, these must be treated according to the commonly accepted rules.

In surgical practice the attempt has been made to remove the disease by suturing the liver to the abdominal walls. Such operations have been performed by Billroth, Tscherning, Marchant, and Richelot. It seems, however, that these operations have never attained any popularity, and probably will not come into general use. As already remarked above, we know indeed that floating liver is commonly one of the phenomena of enteroptosis, and that through an operation (hepatopexy) the original trouble is not removed. Here also, as in the case of floating kidney, I am completely in favor of medicinal treatment—that is, mechanical and dietetic—and am opposed to operative procedures.

THE CLINICAL SIGNIFICANCE OF THIS AFFECTION. From the figures cited by me above it appears that this affection is not of such rare occurrence. Every physician now and then will have occasion to discover cases of floating liver by means of accurate examination, and should, therefore, give this disease his attention. In the second place, recognition of floating liver is of special importance, since otherwise errors in diagnosis may be made which may prove detrimental.

In the last two years I have met in my own practice with four cases of floating liver in which well-known physicians in New York and Philadelphia had been led to make errors in diagnosis. In three cases of floating liver in women the diagnosis of gastric cancer had been made, owing to the presence of a tumor situated below the right border of the ribs and extending toward the left. In one case of floating liver in a man the diagnosis of appendicitis had been made by one physician and of gallstones by another, and both advised urgent resort to operative treatment. The patient, however, soon recovered after the application of a simple abdominal bandage.

The group of cases of floating liver with hepatic colic is often confounded with cholelithiasis. I have certainly observed five cases of this kind in which erroneous diagnoses had been made. One of these cases I reported about six years ago to the Society of Physicians of the German Hospital and Dispensary of New York city. The subject was a man, aged sixty years, who for ten years had frequently suffered with violent colicky pains in the region of the liver, so that injections of morphine had always to be administered for the relief of the attacks. The patient

had gone through all the various gallstone cures, but without the least improvement. Operative procedures had, therefore, been advised by almost every one of the medical men whom he had consulted. The patient, however, objected to an operation, and in the course of his wanderings happened to come to me. I detected a typical floating liver and ordered the patient to wear a well-fitting abdominal bandage, and since that time he has had no further attacks and has enjoyed perfect health.

I cannot, therefore, urge too strongly the diagnostic importance of floating liver, and would further remark that appropriate treatment of this affection is crowned with the most brilliant success in the majority of cases.

**Röntgen Rays for the Detection of Gallstones.** Beck<sup>1</sup> has succeeded in discovering in two patients calculi in the gall-bladder, as well as in the liver, by means of the Röntgen rays. He advises the use of the best Crooke's tubes and a short exposure.

**A Rigorous Milk Diet in Diabetes Mellitus.** Winternitz and Strasser<sup>2</sup> highly recommend a strict milk diet in the treatment of diabetes mellitus. According to these investigators, a strict milk diet effects, after forty-eight hours, in the greater number of diabetic patients, either a disappearance of sugar or at least a considerable decrease of it. Some of the diabetic patients are perfectly cured by this milk diet, and remain well, even when living later on a mixed diet containing a large quantity of amylaceous foods.

**ARSENAURO IN DIABETES MELLITUS.** Barney<sup>3</sup> recommends the use of the double bromide of gold and arsenic, known under the name of "arsenauro." Arsenauero should be given after meals, beginning with five drops and increasing the dose one drop each day until the limit of physiological tolerance is evident—*i. e.*, puffiness about the eyes, a tendency to diarrhoea, and colicky pains about the abdomen. This limit will be reached in some patients at a ten-drop dose, in others at thirty or forty drops.

**Leukæmia.** Kraus<sup>4</sup> reports a case of medullary leukæmia and a large tumor of the spleen, in which the leukæmic symptoms disappeared when the patient had gone through severe infectious diseases, namely, erysipelas, pneumonia, pleurisy, and ultimately peritonitis. The blood returned to an almost normal condition, and so remained until death. This shows the possibility of curing leukæmia in a manner similar to sarcoma.

<sup>1</sup> On the Detection of Calculi in the Liver and Gall-bladder. *New York Medical Journal*, January 20, 1900.

<sup>2</sup> Strenge Milchkuren bei Diabetes mellitus. *Centralbl. f. klin. Medicin.*, 1899, No. 45, p. 1137.

<sup>3</sup> Diabetes Mellitus. *New York Medical Journal*, March 31, 1900, p. 463.

<sup>4</sup> Ein durch eine intercurrente Infektionskrankheit als geheilt zu betrachtender Fall von medullärer lienalen Leukæmie. *Prager med. Wochenschr.*, 1899, No. 42.

# GENITO-URINARY DISEASES AND SYPHILIS.

BY WILLIAM T. BELFIELD, M.D.

## GONOCOCCUS INFECTION.

MANY observations mentioned in this publication last year prove that gonorrhœa is not always nor merely a local disease, but that it is sometimes a blood infection also, with secondary foci in various serous membranes especially, notably the endocardium and synovial surfaces. It is further proven that severe local effects may be produced in parts remote from the infected genitals by the gonococcus toxins alone, the bacteria themselves not entering the blood-current. Both conditions are included in the antique clinical term "gonorrhœal rheumatism."

The morbid processes induced by this affection in joints, muscles, tendon-sheaths, and endocardium have long been clinically identified as of gonorrhœal origin. The gonococcus infection of other serous cavities—peritoneum, pleura, meninges—has been less remotely established; and the proof that the toxins alone cause pleuritis and meningitis is a comparatively recent discovery. The demonstrated gonococcus infection of joints in infants suffering from gonorrhœal conjunctivitis,<sup>1</sup> confirms the suspicion that infantile meningitis must be sometimes ascribed to gonorrhœal as well as to tubercular and syphilitic infection.

Cardile<sup>2</sup> reports the case of a young woman who, while suffering from gonorrhœa, developed pleurisy; aspiration of fluid from the pleural sac showed a pure culture of the gonococcus. No other metastases occurred.

Loeb<sup>3</sup> collects nineteen additional cases (making seventy-three in all) of endocarditis in which the gonococci have been identified in the valvular lesions. In the majority of these cases there was a pre-existing valvular thickening, which seems to favor the settlement on the valves of the gonococci circulating in the blood.

Schiller,<sup>4</sup> incited thereto by Neisser's assertion that gonococci exist on the genitals of women without causing disease, examined the sexual

<sup>1</sup> Transactions of the Royal Medico-Chirurgical Society, 1899; Lucas reports twenty-three cases, eighteen of which were ophthalmia neonatorum.

<sup>2</sup> La Presse Médicale, No. 1, 1900.

<sup>3</sup> Deut. Archiv. f. klin. Med., Bd. lxx., p. 411.

<sup>4</sup> Berliner klinische Wochenschrift, No. xli., 1899.

tract of 300 women taken at random. In fifty-seven he found gonococci ; but every one of these had had some inflammation of the pelvic organs such as is caused by gonococcus infection. Evidence of such inflammation was not discovered in the women whose genitals were free from gonococci.

These observations of Neisser and Schiller, showing that this bacterium may persist in the female sexual canal long after all clinical symptoms of gonorrhœa have subsided, are in accord with the familiar observation that a woman may infect her sexual partner with gonorrhœa even when she herself gives no clinical evidence of the disease ; and she may thus communicate the infection about the time of her menstrual epoch, though the same man may have had relations with her with impunity in the middle of her menstrual month.

Horvath relates two instances in which the gonococcus infection remained limited to paraurethral channels in two cases of hypospadias, the urethra escaping infection in each case ; and Swinburne reports two cases in which infection of paraurethral follicles preceded by several days the evidence of urethral disease. Such cases are additional explanations of the mysterious transfer of gonorrhœa by individuals who, on cursory examination, are apparently free from it.

**Treatment.** The agent which, carried by the blood-current to all parts of the genital canal, shall arrest the multiplication of the gonococcus in the walls of that canal remains undiscovered. The only remedy for which such claims have been made in the past year is methylene-blue. Some observers ascribe to this specific, administered in one-grain doses four times daily, the power of curing a gonorrhœa in three to five days. In a fair number of cases under my observation this remedy failed to disclose such power or even any marked influence in combating the disease. Probably some of the cases reported as promptly cured by it were not fresh gonococcus infections, but rather auto-infections from the deep urethra or even non-gonorrhœal infections. Failure to distinguish between freshly acquired gonorrhœa on the one hand, and the various other causes of urethritis on the other, is well known to be responsible for many erroneous deductions in urethral therapeutics.

Methylene-blue, when given internally in the treatment of gonorrhœa or for any other purpose, should be combined with oil of nutmeg, which prevents the irritation of the bladder neck caused by the blue alone. Each capsule may contain :

|                             |          |
|-----------------------------|----------|
| Methylene-blue . . . . .    | 1 grain. |
| Oil of nutmeg . . . . .     | 1 drop.  |
| Oil of sandalwood . . . . . | 1 drop.  |

One capsule may be given after each meal and at bedtime.

**LOCAL TREATMENT.** Injections and irrigations still constitute our chief reliance in the treatment of gonorrhœa; the agents which have been found most useful in this way are hot-water, the yellow salts of hydrastis, protargol, and potassium permanganate.

The so-called Janet irrigation method with permanganate solutions has failed to secure in most hands the brilliant results published by its ardent advocates; indeed, it seems probable that the chief benefit is conferred by the hot-water irrigation of the entire urethra rather than by the dissolved salt; and that the substitution of hydrastis or protargol or both for the permanganate secures better results than the Janet method. In the acute stage I use injections (of the anterior urethra only prior to the tenth day of the disease) of the following:

|                              |   |   |   |   |   |   |           |
|------------------------------|---|---|---|---|---|---|-----------|
| R.—Hydrast. muriate (yellow) | . | . | . | . | . | . | gr. v.    |
| Protargol                    | . | . | . | . | . | . | gr. v.    |
| Glycerinæ                    | . | . | . | . | . | . | ʒss.      |
| Aquæ dest.                   | . | . | . | . | . | . | ad ʒj.—M. |

The patient makes this injection four to six times daily, retaining the fluid five to ten minutes each time. This injection is preceded, when practicable, by a hot-water injection.

When the symptoms indicate the extension of the infection into the deep urethra (usually not before the eighth day) the patient is taught to inject the entire urethra, using at least an ounce for each injection. For these irrigations the same solution may be profitably used, or the potassium permanganate, 1:4000. It is only after the acute stage has passed (say after the tenth day) that the Janet method should be used, if indeed it is used at all. It has been quite largely abandoned, because of both its inefficiency and its tendency to provoke inflammation of the deep sexual organs.

**Treatment of Chronic Gonorrhœa and Gleet.** The treatment of these disorders consists chiefly of the three local measures—milking or massage of the prostate and vesicles, irrigation of the entire urethra, and the passage of large sounds (up to No. 19 or 20 of the English scale). Internal medication—consisting of the balsams, santal oil, etc.—seems of little value.

For irrigation of the deep urethra the most efficient are silver nitrate (1 grain to 8 ounces), yellow hydrastis muriate (1 grain to the ounce), zinc chloride or permanganate (1 grain to the ounce), potassium permanganate (1 grain to 8 ounces), and picric acid (1 grain to 2 ounces). These are initial strengths; the proportion of salt to water may be increased at subsequent sittings. Two to four ounces of the solution should be injected from the meatus to the bladder, and then expelled by the patient. Picric acid which I have used and recommended for

years has been recently warmly commended by Desnos.<sup>1</sup> He instilled 20 to 80 drops of a solution varying from 2 to 5 grains to the ounce, using it every second day in cases of chronic and tubercular urethritis. He reports a complete cure in each of seventeen cases of simple urethritis and in two out of twelve cases of tubercular urethritis. This is a larger percentage of cures than has attended my use of this agent, which is, however, of decided value.

**DILATORS.** The great value of stretching strictured and indurated parts of the urethra in the treatment of gleet is well shown by the benefit following the passage of large sounds. Such stretching and massage of indurated spots is still more efficiently and accurately accomplished by the use of various urethral dilators. These may be introduced through a meatus which prevents the entrance of a large sound; and the diseased part may be overstretched—*i. e.*, dilated beyond the usual calibre—without subjecting the healthy parts, including the meatus, to this strain. Such treatment has in certain cases a pronounced effect.

**Abortive Treatment of Gonorrhœa.** A recent recommendation for securing the ardently desired abortive treatment of a gonorrhœa is that of Motz and Nogues to the French Congress of Urology: 1. Immediate irrigation of the anterior urethra with potassium permanganate solution, 1:500. 2. Twelve hours later irrigation of the anterior urethra with a solution of the same remedy, 1 part in 1000 parts of water, and of the deep urethra with 1 part in 2000. If the secretion becomes thin and is diminished in quantity, continue to irrigate the entire urethra twice daily with the solution containing 1 part in 2000; otherwise continue the use of 1 part in 1000 until four irrigations with it have been given. All this must be done before the reactive inflammation becomes pronounced.

While I have had no experience with this method, it does not impress me as rational or commendable. To irrigate the deep urethra against bacteria that are still confined to the anterior part of this channel seems devoid of benefit, but not of danger. The advice savors of the urethral irrigation frenzy from which our French colleagues are still suffering.

If any attempt at aborting a gonorrhœa is made it should consist of the instillation into the fossa navicularis—at the earliest possible moment after suspicious reddening of the meatus and microscopical confirmation of the diagnosis—of 8 or 10 drops of a silver nitrate solution, 5 grains to the ounce. This is always justifiable, and perhaps occasionally successful.

**Treatment of Gonorrhœal Arthritis.** We possess no remedy which exhibits a distinct power to inhibit the growth of gonococci in the

<sup>1</sup> La Presse Médicale, No. lvi., 1899.



blood-current or in the tissues; hence, the treatment of gonorrhœal arthritis is still tentative and unsatisfactory. My best results have followed the inunction of the following:

R.—Guaiacol . . . . . ℥j.  
 Ol. olive . . . . . ℥ij.—M.  
 Rub a teaspoonful into the skin over the inflamed joint four times daily.

If several joints are infected each may receive an inunction, provided the total daily dose does not exceed four teaspoonfuls of this mixture. The anæsthetic effect of the guaiacol is very gratifying.

In some recent cases I have added to this the inunction of mercurial ointments as used in the treatment of syphilis. This has been warmly recommended in the treatment of gonorrhœal arthritis by Schuster,<sup>1</sup> on the basis of ten years' experience. I deem it worthy of further trial.

## TUBERCULOSIS.

In the earlier days of applied bacteriology the surgeon's eye was fixed upon the pathogenic bacterium, and his efforts were directed solely to the destruction of the invading parasite. Mosetig-Moorhof's introduction of iodoform as a surgical dressing in 1881 not only furnished a valuable weapon against surgical infections, but also laid the foundation for a more rational surgical pathology: it directed attention to the soil as well as to the plant, to the invaded tissues as well as to the invading bacteria. As a result there has been a gradual but profound trend of surgical practice toward conservatism in the treatment of bacterial infections—the spray, carbolic acid, bichloride of mercury and other toxic antiseptics have been banished from the treatment of fresh wounds.

In the treatment of tuberculosis this conservatism has been especially marked in recent years; excision of joints and other mutilating operations have been largely superseded by iodoform injections and other measures tending to conserve and invigorate rather than to destroy. Surgery has aimed to assist the tissues in fighting the tubercle bacilli rather than to directly destroy these organisms.

This tendency of surgical practice has become manifest in the attitude of genito-urinary surgeons toward tuberculosis of the male genital organs: excision of the testicle for tuberculosis of the epididymis is now generally condemned and replaced by excision of the tuberculous tissues alone, while tissue resistance is encouraged by hygienic measures. Roux's extirpation of the tuberculous seminal vesicle, cord, and testicle has found but few advocates, and curetting of the tuberculous bladder is not generally practised.

<sup>1</sup> Journ. Méd. de Brux., 1899, No. 29.

**Raw Meat in the Treatment of Tuberculosis.** An innovation in the treatment of tuberculosis, both medical and surgical, that deserves more than a passing notice, is the addition of raw meat to the diet. The idea is, of course, not a novel one; the fact that carnivorous animals are in general refractory, herbivorous susceptible, to the tuberculous infection, has suggested to many minds the possible value of a flesh diet in the prevention and cure of that disease. Indeed, in 1865, Fuster in Paris reported favorable results from the use of raw meat and alcohol as a diet for consumptives. It remained, however, for Sicard and Martin<sup>1</sup> to establish by extended and systematic research, both experimental and clinical, the actual value of raw meat as a remedy for animals and men afflicted with tuberculosis. According to their prolonged and accurate observations, the addition of two to four ounces of raw meat to the daily food of the tuberculous patient is an extremely valuable aid. Sicard's experimental work shows that the benefit is not obtained from cooked meat; only the raw food has the desired effect. Richet and Héricourt achieved similar results, and ascribe them not to forced feeding, but to an antitoxic quality of raw as distinguished from cooked meat.

While the results of this treatment have not been recorded by others, the character of the work done by Sicard and Martin independently commends the further trial of this remedy.

**Tuberculosis of the Kidney.** In just one location has genito-urinary surgery become more radical in its attitude toward the tubercular infection, namely, when invading the kidney as a primary disease. Many operators have recorded most favorable results, remote as well as operative, following excision of the kidney for primary tuberculosis. Schmierer<sup>2</sup> reviews 205 articles on this subject, showing the essential unanimity among surgeons of experience in advising retroperitoneal nephrectomy. Albarran advises against the operation if the infection has involved also the renal pelvis—advice not generally indorsed. Koenig<sup>3</sup> gives his conclusions from a large experience in renal tuberculosis: resection and nephrotomy are virtually worthless; nephrectomy is the one remedy. He performs this operation, though nodules in the epididymis, vesicle, or prostate prove infection of the genital organs; even when the opposite kidney is somewhat infected he does not fear to remove the more extensively diseased one, for even under these circumstances he has seen removal of the tuberculous kidney followed by marked local as well as general improvement, sometimes a symptomatic cure.

<sup>1</sup> La Presse Médicale, June 13, 1900.

<sup>2</sup> Centralbl. f. d. Grenzgeb. d. Med. und Chir., 1899, Bd. ii.

<sup>3</sup> Deutsche med. Wochenschr., 1900, No. 7.

He admits the difficulty in determining that essential point—the functional condition of the opposite kidney. For this purpose he relies upon vesical cystoscopy and manual examination. The absence of tubercle bacilli from the urine examined is not unusual, especially in tuberculous pyelitis. Koenig refrains from catheterization of the ureters in tuberculous cases, and does not trust either the Koranyi method of blood freezing or the renal permeability to dyes as an index to the functional activity of the opposite kidney.

In the discussion of this subject at the Paris Société de Chirurgie,<sup>1</sup> Albarran's long experience was adduced to show that in his hands, at least, catheterization of the ureter is quite safe, even when the urinary tract is the seat of the tuberculous infection.

In this connection, a case of Braatz<sup>2</sup> is of interest: A woman, aged thirty years, with symptoms of tuberculosis, experienced colicky pains over the right kidney, which was found to be movable. Nephropexy was performed, with transient palliation only; then splitting of the kidney (which seemed normal) was followed by complete cure, lasting three years. At the end of this period recurrence of the pain caused nephrectomy. New tuberculous nodules were found in the upper end of the excised kidney and an old, encapsulated nodule at the lower end. Braatz suggests that the splitting of the kidney three years earlier had caused the healing of the old tuberculous focus and consequent relief of pain.

Nephrectomy is, then, the preferred treatment for primary renal tuberculosis, provided the patient's general condition and the functional performance of the opposite kidney render survival of the operation a distinct probability.

Tuberculosis of the bladder and the genital organs is treated conservatively when possible, débris of tissue being removed and the general health invigorated.

The frequency of genito-urinary tuberculosis is indicated by Posner's observation in Virchow's laboratory, where 5 per cent. of 1300 necropsies showed this infection, and in 70 per cent. of these the tuberculosis was primary in the genital or urinary organs; in other words, 3.5 per cent. of all necropsies showed primary genito-urinary tuberculosis.

**Identification of Tubercle Bacilli in the Urine.** In no other locality is the identification of these bacilli beset with more difficulties or possibilities of error than in the examination of the urinary sediment. It has long been known that repeated expert examinations have failed to detect these bacteria in the sediment from cases where typical clinical

<sup>1</sup> La Semaine Méd., June 20 and 27, 1900.

<sup>2</sup> Deutsche med. Wochenschr., 1900, No. 10.

symptoms were confirmed by operation or necropsy. On the other hand, certain other bacteria, especially that frequent inhabitant of prepuce and vulva—the smegma bacillus—can be and certainly have been mistaken for tubercle bacilli, because they are stained by the manipulations established for the latter. Unusual caution must, therefore, be observed in reaching the conclusion that bacteria found in the urine are really Koch bacilli, while failure to find such does not vitiate a clinical diagnosis of urinary tuberculosis. Guyon's teaching that persistently purulent urine in which no bacteria can be detected probably proceeds from a tuberculous urinary tract is wisely conservative.

The laboratory methods for identifying tubercle bacilli in urine are carefully discussed by Sondern.<sup>1</sup> He states that probably 40 per cent. of 6000 urinary sediments that he has stained with carbol-fuchsin have shown smegma bacilli; furthermore, unlike other observers, he has found them in urine drawn by catheter, and even in urine proceeding directly from the ureter through the ureteral catheter. He considers prolonged decolorization by alcohol the best treatment for differentiation between the tubercle and smegma bacilli; after the carbol-fuchsin stain and decolorization by nitric acid the glass is immersed in absolute alcohol five to eight hours, whereby the color is removed from smegma but not from tubercle bacilli.

Sondern also warns against the mistaken conclusions incident to the inoculation test in animals.

### ACTINOMYCOSIS.

This infection has been recognized in the genito-urinary tract but rarely, and then only secondary to disease of the surrounding organs. Israel<sup>2</sup> reports a primary actinomycosis of the kidney; the chief symptom was hæmaturia, because of which nephrotomy had been performed six years earlier, without, however, arresting hemorrhage or affording a diagnosis. Israel discovered the actinomyces in the urine, and removed the kidney; the plant was found in the kidney and renal pelvis, and concretions had formed around the parasitic masses.

Leger<sup>3</sup> observed a case of stubborn gleet discharge, with suppuration in the glans penis; actinomycetes having been detected in the pus, amputation of the glans was performed, followed by prompt healing.

**Treatment.** Actinomycosis, wherever located, is distinctly amenable to treatment by potassium iodide; many cases of extensive infection have

<sup>1</sup> *Journal of Cutaneous and Genito-Urinary Diseases*, July, 1900.

<sup>2</sup> *Berliner klin. Wochenschr.*, 1899, No. 51.

<sup>3</sup> *Annales d. Maladies d. Org. Genito-Urin.*, May, 1900.

been promptly healed by the internal administration of 1 to 2 drachms of the salt daily ; others have been refractory to this treatment, but have yielded when to the internal use was added the local subcutaneous injection of weak solutions of the iodide. The value of these local injections, first emphasized by Rydygier,<sup>1</sup> has been recently illustrated in several cases by Sawyers,<sup>2</sup> who is the first, so far as I am aware, to successfully treat pulmonary actinomycosis by such injections. This patient, a stock-raiser, aged fifty-three years, steadily failed for six weeks under the internal administration of the iodide, but immediately began to improve when intrapulmonary injections—30 to 60 minims of a 1 per cent. solution—were made into the diseased tissue every third day. After twenty-five injections his weight had increased from 105 to 155 pounds, and his health was completely restored.

### PUS INFECTIONS.

To the pyogenic bacteria which may infect the genito-urinary organs has been added the pneumococcus. Guillon<sup>3</sup> observed a prostatic abscess develop in an elderly patient after an attack of bronchopneumonia. The pus proved to be a pure culture of the pneumococcus. Welch mentions the discovery of his *B. aërogenes capsulatus* in one case of cystitis.

The chief interest in the pyogenic infections of these organs centres in the therapy, and most prominent among medicinal agents against them remains urotropin. Many articles confirming the value of this agent have appeared ; they have been summarized in the *Centralblatt für Krankheiten der Harn. und Sexual Organe*, for May, 1900. Orlovsky publishes also a careful and exhaustive experimental study of urotropin, the results of which accord with the general clinical observations. The consensus of opinion during the past year corroborates the estimate of urotropin given in PROGRESSIVE MEDICINE a year ago (Vol. IV., p. 114), namely, that it is the best known agent for combating pus infections of the urinary tract ; that its action is especially noteworthy when the urine is ammoniacal ; that it promptly arrests the multiplication of the colon and typhoid bacilli as well as of the ordinary pyogenic bacteria ; that it often removes the symptom phosphaturia, possibly by effecting a change in metabolism. It has no appreciable effect in retarding the multiplication of the gonococcus or tubercle bacillus, and it has no demonstrable value in dissolving urinary concretions.

Groszlick<sup>4</sup> details clinical experience with urotropin which leads him

<sup>1</sup> Wiener klin. Wochenschr., September 12, 1895.

<sup>2</sup> Transactions of the Iowa State Medical Society, 1900.

<sup>3</sup> Annales d. Maladies d. Org. Gen.-Urin., February, 1900.

<sup>4</sup> Centrabl. f. Krank. d. Harn. und Sex. Org., May, 1900.

to the conclusion that its value as a urinary antiseptic is no greater than that of salol and boric acid ; that its effect ceases when the administration of the drug is discontinued, and that it is virtually useless in chronic infections of the urinary tract as well as in phosphaturia, the effects being transient. His article is noteworthy because at variance with the general experience.

Nicolaier's<sup>1</sup> lengthy article reviews our present knowledge of urotropin, but adds nothing noteworthy except its failure to influence a streptococcus infection in one case.

### CALCULI.

The only notable work of the year pertaining to urinary concretions relates to diagnosis by means of the Röntgen rays. That short exposures facilitate the detection of small renal calculi was proven in the work of Braatz, Abbe and others, reviewed a year ago;<sup>2</sup> but this work left much to be desired in the detection of calculi composed of uric acid and its compounds. The status was that while the Röntgen rays might afford the only available proof of the existence of small calculi, yet they might fail to picture calculi, even of considerable size, which were composed of uric-acid compounds.

The work of Leonard,<sup>3</sup> if found correct, will vastly increase the value of the X-rays in the recognition of urinary concretions ; indeed, we shall possess absolute diagnostic ability as to the absence as well as the presence of calculi in kidney and ureter. Leonard uses Crooke's tubes of various vacuum degrees ; with those of low vacuum he asserts the ability to detect small stones of whatever composition. He has pictured in the kidney a calculus weighing only nine-tenths of a grain ; crystals not yet agglutinated into a concretion were also detected and removed. He affirms the absence of a stone with quite as much confidence as its presence ; in six out of seven cases where the symptoms indicated a renal calculus, operation proved his negative diagnosis correct ; his one mistake, he asserts, was due to faulty technique.

The importance of early diagnosis, both positive and negative, as to the presence of calculi in kidney and ureter is obvious ; such diagnostic ability will greatly simplify a difficult problem in renal surgery. As yet no other investigator has repeated Leonard's work, and we are not prepared to accept his experience as final without corroboration.

**Calculi in the Ureter.** Two articles on calculi in the ureter are furnished by Morris<sup>4</sup> and Newman,<sup>5</sup> in which the variation in symptoms

<sup>1</sup> *Zeitschrift f. klin. Med.*, Bd. xxxviii.

<sup>2</sup> *PROGRESSIVE MEDICINE*, Vol. IV., p. 128.

<sup>3</sup> *Journal of the American Medical Association*, July 21, 1900.

<sup>4</sup> *Lancet*, December 16, 1899.

<sup>5</sup> *British Medical Journal*, April 21, 1900.

and clinical history are fully set forth. Cases are recorded in which the symptoms of ureteral calculi have been quite excusably misinterpreted as indicating disease of the gall-bladder, pylorus, kidney, appendix, ovary, and tube. The appendix often lies directly over the lower segment of the ureter, in which calculi are prone to be arrested. The Röntgen rays may well here afford great service, as illustrated in Tuffier's article last year.

**GLYCERIN AS A REMEDY FOR LITHIASIS.** The internal administration of glycerin in teaspoonful doses is recommended by Hermann.<sup>1</sup> He has observed 115 cases, in 15 of which a calculus was passed while the patient was taking glycerin; in 25 distinct improvement of symptoms was observed.

That ligatures and sutures may be found as nuclei of vesical calculi after operations which do not open the bladder is a curious but well-attested observation. Operations on the tubes in women and for hernia in men seem most apt to be followed by migration of the silken knots into the bladder and subsequent calculus formation.

## KIDNEY.

**Surgical Treatment of Unilateral Nephritis.** A recent important advance in knowledge of renal diseases is the discovery that nephritis, especially that due to bacterial infection, is often unilateral. The first intimations of this conception arose from the various exploratory operations undertaken to discover the cause of symptomless or "essential" renal hæmaturia and persistent nephralgia. In most of the cases in this category operated in recent years in which sections of the kidney tissue were examined by the microscope, there was found either a chronic nephritis or an infection of kidney tissue or renal pelvis; and the complete arrest of bleeding or pain following nephrectomy or nephrotomy in these cases showed that the morbid condition was unilateral. This fact has been further confirmed by the ureteral catheter.

Harrison, after curing three cases of subacute infectious nephritis by splitting the capsule, proposed this measure as the treatment for this condition. Nélaton and Körte practised it independently for the relief of congestive anuria,<sup>2</sup> and various surgeons have successfully followed Harrison's advice. The largest experience by one operator is that of Pousson, who reported to the French Congress of Urology twelve cases of operation for acute and subacute infectious nephritis—nine nephrotomies, three nephrectomies—with ten cures and two deaths.

<sup>1</sup> Medical Chronicle, January, 1900.

<sup>2</sup> PROGRESSIVE MEDICINE, 1899, Vol. IV.

Edebohls<sup>1</sup> performed nephropexy on 118 patients. In six of these the usual symptoms of chronic nephritis existed at the time of operation ; in four of the six all symptoms of renal disease disappeared within a short time thereafter ; in one the kidney remained movable and the nephritis continued. In the four cured cases the nephritis was unilateral.

Present experience may be thus summarized :

1. Nephritis, especially that due to bacterial infection, frequently affects one kidney only.
2. It is sometimes accompanied by persistent hæmaturia or renal pain, or both ; while the clinical and urinary features considered typical of nephritis may be absent.
3. The ureteral catheter or (in case of hæmaturia) the cystoscope may determine the limitation of the lesion to one kidney.
4. Relief of tension by splitting the kidney capsule or by nephrotomy usually effects a cure ; sometimes nephrectomy is necessary.
5. Arrest of renal secretion, due to renal congestion, has been cured by simple nephrotomy.

**Essential Renal Hæmaturia.** In *PROGRESSIVE MEDICINE*, 1899, Vol. IV., it was remarked that later and more careful observation of these cases had in nearly all removed the mystery that formerly surrounded this symptomless bleeding ; that in most cases there exists either chronic nephritis, congestion of the kidney (from movable kidney or other cause), incipient tuberculosis, or other bacterial infection ; that the "angioneurotic" hypothesis—which, after all, was merely a cloak for earlier ignorance—was fast falling into disrepute.

While that review was in press the French Congress of Urology met in Paris under the presidency of Guyon and exhaustively discussed this topic. The almost unanimous opinion was that an "angioneurotic" bleeding does not exist ; that the hæmaturia is always the result of local morbid processes, chief among which are chronic nephritis, floating kidney, hydronephrosis, and early tuberculosis. Albarran reported another case of hæmaturia relieved by nephrotomy, an excised piece of the kidney showing diffuse nephritis without the accepted urinary changes or clinical symptoms. Guyon mentioned two additional cases (there are now twelve recorded) of hæmaturia during pregnancy ; he thinks these also are due to mechanical and inflammatory conditions. Boursier remarked that oxalate and urate crystals too small to be considered calculi may cause hæmaturia, especially in children after digestive disturbances. (I operated and reported<sup>2</sup> a case of renal hemorrhage

<sup>1</sup> Medical News, April 22, 1899.

<sup>2</sup> Journal of the American Medical Association, May 7, 1887.



from uric-acid crystals in 1887.) It is certain, too, that early tuberculosis of the kidney may be the sole cause of symptomless hæmaturia.

**TREATMENT.** It was the opinion of the Congress that surgical treatment only is effectual—nephrotomy usually succeeding, nephrectomy being occasionally necessary—and such was the conclusion expressed in this review last year. It is, however, possible that the bleeding from cases of nephritis may sometimes be arrested by gelatin solutions injected subcutaneously.

**THE HÆMOSTATIC EFFECT OF GELATIN.** That gelatin warmed to fluidity and applied directly to a bleeding surface is our most efficient styptic is a recent and valuable discovery; the hæmostatic effect of subcutaneous injections on remote hemorrhages (from lungs, kidneys, uterus) has been less uniform, but sometimes strikingly good. I have reported<sup>1</sup> a case in which an "essential" renal hæmaturia of two years' standing was promptly arrested by such injection, after the usual hæmostatics had failed. The solution used was that originally employed by Lance-reaux in the treatment of aneurism: Gelatin, 20 parts; sodium chloride, 7 parts; distilled water, 1000 parts; sterilized by boiling. Two to four ounces of this were injected subcutaneously and the injection repeated several days later.

Schwabe<sup>2</sup> records a case of recurrent nephritis with severe hæmaturia. After various other hæmostatics had been tried in vain, 25 c.c. of a 2 per cent. gelatin solution were injected below each clavicle; half a litre of a 10 per cent. solution was given daily by the mouth for a week. The bleeding promptly stopped.

Freudenweiler<sup>3</sup> reports two cases of hemorrhagic nephritis in which the use of gelatin not only failed to check the loss of blood, but was also followed by an increase in the urinary albumin and casts, decrease in the amount of urine and hæmoglobinuria.

It would seem, therefore, that so-called essential renal hæmaturia should be submitted to this treatment before surgical means are employed, though experience must show which of the pathological conditions accompanied by renal hemorrhage are amenable to such treatment.

## URETER.

Morris,<sup>4</sup> in twenty-six cases of hydronephrosis, found the cause in the obstruction in the ureter through valvular formations of mucous membrane, strictures, twisting, calculi, and compression. He advises resection of the ureter in such cases, since attempts to remedy the local conditions by catheterization are seldom successful.

<sup>1</sup> Chicago Medical Recorder, April, 1900.

<sup>2</sup> Therap. Monatshefte, June, 1900.

<sup>3</sup> Deutsche med. Wochenschr., July 7, 1900.

<sup>4</sup> Lancet, December 16, 1899.

Dudley<sup>1</sup> reports a valuable and suggestive case: A woman aged thirty-seven years, had been troubled since the birth of a child, twenty-one years earlier, with dysmenorrhœa, leucorrhœa, and pain in the left inguinal region of varying intensity, making her a semi-invalid. Cervix and perineum were found lacerated and were repaired. Hemorrhage, occurring several days later, required deep sutures in the parametrium. A resulting urinary fistula led to examination of the ureter and discovery of an old stricture with dilatation above. A new vesico-ureteral orifice was ingeniously and safely made by pressure-necrosis by means of forceps. The inguinal pain ceased permanently.

Dudley suggests the possibility that lacerations during delivery may not infrequently be the cause of ureteral strictures, and these in turn may occasion aches and pains attributed to the obvious laceration, but often not relieved by repair of the latter.

**Operations upon the Ureter.** The conditions described in Morris' article and various others may permanently interfere with the passage of urine from the kidney to the bladder. The earliest remedies for this condition were nephrectomy and a uretero-cutaneous fistula. These have been in recent years succeeded by attempts to repair the ureter, or to make it debouche into the bladder or bowel. MacMonagle<sup>2</sup> reviews the literature of this subject and the operations that have been successfully performed:

1. Resection of the ureter with anastomosis between the cut ends has been successfully practised in about twenty cases, transverse and oblique end-to-end anastomosis being the favored operations. As the ureter can be separated from the peritoneum for several inches without impairment of vitality, and as the cut ends can be stretched considerably, a defect of even two inches can be overcome by such anastomosis.

2. Implantation of the ureter into the bladder—best intraperitoneally—has been practised successfully, usually for fistula in the lower segment. Sokoloff<sup>3</sup> collects twenty-seven cases and adds one of his own; in three the result was fatal.

3. Implantation of the ureter into the intestine, the Maydl method being preferred, has become a standard operation. Peterson<sup>4</sup> gives an exhaustive review of the literature of this subject, with some original experimental observations.

Beck<sup>5</sup> excised the bladder for tuberculosis, and sewed the ureters into the sigmoid flexure so that one and a half inch of each projected into

<sup>1</sup> Boston Medical and Surgical Journal, March 1, 1900.

<sup>2</sup> American Journal of the Medical Sciences, 1899, p. 684.

<sup>3</sup> Deutsche Zeitschrift f. Chir., 1899, p. 185.

<sup>4</sup> New York Medical Record, vol. lvii., No. 20.

<sup>5</sup> Chicago Medical Recorder, December, 1899.

the bowel, hoping thereby to diminish the danger of infection. The patient was still free from nephritis several months later.

Bovée<sup>1</sup> also gives a critical review of ureteral implantation.

## BLADDER.

**Infantile Bladder.** Haven<sup>2</sup> relates two cases of infantile bladder in girls, aged seventeen and eighteen years, the organs holding only three to four ounces, and the patients having incontinence of urine. By means of warm-water injections the bladder capacity was gradually increased to twelve or sixteen ounces, and the incontinence ceased. This is a valuable method for treating incontinence in young persons of either sex.

**Tumors of the Bladder.** The malignant tendency of bladder tumors, even those apparently benignant at the time of operation, has been the subject of frequent remark. Albarran and Clado followed the histories of 110 cases operated for benignant growths, and found 85 permanent recoveries; of 208 malignant cases 51 recovered.

Motz followed the history of thirty-five cases operated for bladder tumor at the Necker Hospital. Ten of these were alive three years or more after operation. These 10 comprised 1 case of epithelioma out of 18 operated, and 9 cases of papilloma out of 17 operated; of these 9 cases 4 showed a recurrence of the growth. Thus of the thirty-five cases only six gave promise of permanent freedom from the growth—results which accord with the general impression as to the probability of recurrence after operation for bladder tumors.

**Ulcer of the Bladder.** The bladder—like that other organ the stomach, whose contents are frequently acid—may be the seat of a “simple” ulcer—*i. e.*, one due to no known infection. This is a fact that has received but scant recognition at the hands of surgeons, perhaps because the proof thereof has not been voluminous. Hence, especial interest and importance attaches to the report by Castaigne<sup>3</sup> of a case of ulcer of the bladder, with necropsy; the particularly valuable feature is the proof that the simple ulcer of the bladder, like that of the stomach, may perforate the entire thickness of the wall of the organ, permitting the escape of the visceral contents into the peritoneal cavity, and consequent fatal peritonitis. Castaigne’s patient was a healthy man, aged thirty-six years, who seven days prior to death was seized with severe pain in the lumbar region, radiating thence to the testicles and penis especially; severe vesical irritation and hæmaturia, becoming pro-

<sup>1</sup> *Annals of Surgery*, August, 1900.

<sup>2</sup> *Boston Medical and Surgical Journal*, June 15, 1899.

<sup>3</sup> *Annales des Maladies des Organes Gen.-Urinaire*, March, 1900.

fuse, followed two days later, and continued almost to death ; peritonitis developed prior to the fatal ending.

A careful examination made thirty hours after death revealed a perforating ulcer in the posterior-superior region of the bladder ; it was of oval outline, about 2 cm. in the transverse and 1 to 1.5 cm. in the vertical diameter at the mucous surface, its area diminishing as it approached the peritoneal covering. Expert histological examination of sections proved the absence of tuberculosis and cancer. The other organs were normal.

There remains only the possibility that the ulcer was of syphilitic origin—a contingency not discussed and apparently not remembered by the observer. But the history of rapid progress and the observation of similar cases render it practically certain that such ulcers occur independently of the syphilitic infection.

The clinical importance of a general recognition of this morbid condition is obvious ; the excellent results that have attended the efforts to repair ruptures of the bladder, and the ease with which peritoneal infection by the urine can be averted, made it reasonable to assume that the prompt recognition of this condition and immediate attempt to relieve it will be followed by better results than those—by no means discouraging—which have attended the surgical relief of perforating ulcer of the stomach.

**Typhoid Infection of the Bladder.** In last year's review were mentioned the observations of Horton Smith, Richardson, and Gwyn, who described the occurrence of typhoid bacilli in the urine with some cases of obstinate cystitis of several years' duration due to this bacterium. The internal administration of urotropin was followed by the immediate disappearance of the bacilli and arrest of cystitis. In all of these cases the urine and urinary tract had been infected from the blood-current, and in all but one the patient had suffered from typhoid fever shortly before the urinary infection was noticed. Browne<sup>1</sup> reports a case of typhoid bacillus infection of the bladder apparently by another route—the catheter. The patient, who had always been free from cystitis, underwent an operation for uterine fibroids, after which she required catheterization. A few days later she developed cystitis, and the urine was found to be a culture of the Eberth bacillus. The patient had no other sign of typhoid fever, but had had an attack thirty-five years earlier.

The case has an obvious clinical lesson, and adds another to the already considerable number in which infection of various tissues by the typhoid bacillus has occurred without intestinal lesions.

<sup>1</sup> New York Medical Record, March 10, 1900.

**Treatment of Cystitis.** The many additions to our knowledge of bladder disease—which we owe especially to cystoscopy and bacteriology—have taught the lesson that cystitis is not an entity, to be treated as such, but merely the result of various bacterial infections. The first item in the treatment of cystitis is to detect the cause; the second, to remove that cause if possible. The most frequent of the infecting agents are (1) urea-decomposing bacteria, (2) the colon bacillus, (3) the gonococcus (usually limited to the bladder-neck, (4) the tubercle bacillus.

The pyogenic bacteria (urea-decomposers and colon bacillus) seem incapable of invading the tissues of a healthy bladder; they are found when the vitality of the vesical lining has been impaired through stone formation, enlarged prostate, tight stricture, etc. Their presence is, therefore, a signal to search for these pre-existing causes before beginning treatment. The agents which subdue the secondary infection or cystitis are urotropin and salol internally and weak solutions of silver nitrate (1: 4000 or 1: 8000) locally; but the important feature in treating cystitis remains always the search for the cause, and this implies a bacteriological examination of the urinary pus as well as investigation as to stricture, stone, etc. Among the empirical measures sometimes useful in the treatment of painful and spasmodic affections of the bladder whose cause is obscure, is the forcible dilatation of the anus.

**Bleeding from the Bladder.** Hemorrhage from the bladder may be caused by a calculus, tumor, tuberculous or other ulcer, bladder hemorrhoids, etc.; the treatment is naturally determined by the nature of the cause, which is often determinable only through the cystoscope. There are two therapeutic measures frequently useful: the intravesical injection of weak silver nitrate solutions and the subcutaneous injection of gelatin solutions. Silver nitrate—1 grain to a pint of water at first, gradually increased to double that strength—has a distinct styptic effect in the bladder, even when the bleeding proceeds from papillomata; 2 or 3 ounces of such a solution may be gently injected and then expelled by the patient. The daily use of such an injection for a month or more is very serviceable, provided the hemorrhage does not proceed from tuberculous tissues, which are injured by it. These injections should be so dilute as not to provoke spasmodic contractions of the bladder, which usually vitiate the styptic effect.

The intravesical injection of gelatin solution has been tried by others as well as by myself without success; but the subcutaneous injection of a 2 per cent. gelatin solution in normal saline liquid (20 parts gelatin, 7 parts sodium chloride, and 1000 parts distilled water, sterilized by boiling) I found efficient in a test case.<sup>1</sup> Here various local and internal

<sup>1</sup> Chicago Medical Recorder, April, 1900.

remedies had failed to arrest bleeding from a malignant growth ; a single subcutaneous injection of 4 ounces of the solution named was followed by prompt and permanent arrest of the hemorrhage.

The boiling for sterilization should be brief (not more than five minutes), because the changes produced in gelatin by prolonged boiling probably destroy its hæmostatic properties.

A third valuable remedy for intravesical bleeding is the injection of antipyrine ; 2 to 4 ounces of a 10 per cent. watery solution may be injected and allowed to remain fifteen minutes, then withdrawn.

## PROSTATE.

**Malignant Tumors.** Wolff<sup>1</sup> collects and reviews the literature of sarcoma and carcinoma of the prostate. One of the interesting cases is that in which cystitis caused by an apparent senile hypertrophy was improved by double castration in June, 1896. Some months later the symptoms returned and the prostatic enlargement increased. In September, 1897, the autopsy showed that the enlargement was carcinomatous. The case illustrates two established clinical facts : (1) That carcinoma may be mistaken, in its earlier stages, for the more frequent senile enlargement ; and (2) that castration has no effect on cancerous disease of the prostate.

Albarran and Halle<sup>2</sup> present an elaborate anatomical and clinical study of the senile prostate. In 14 of 100 prostates examined histologically they found more or less distinct atypical departure from the usual adenomatous structure. They maintain that between simple hypertrophy and typical carcinoma there is a semi-malignant growth of adenoma which has not yet secured clinical recognition ; it is, in fact, the transformation stage. Their contention is amply supported by general clinical experience.

The operative treatment of malignant disease of the prostate has not as yet progressed beyond palliative measures ; total excision, performed in less than a score of cases, has been in every instance either immediately fatal or followed by fatal recurrence within a year. The anatomical difficulties, together with the early metastasis of prostatic cancer to bones, offer obstacles hitherto insuperable to the permanent cure of this condition.

**Senile Enlargement of the Prostate.** The literature of this subject shows that the various operations, more or less irrational, which have been vaunted for the relief of this condition, are receiving more intelligent and less enthusiastic consideration.

<sup>1</sup> Deutsche Zeitsch. f. Chir., Bd. lii., p. 336.

<sup>2</sup> Annales d. Mal. d. Org. Gen.-Urin., February and March, 1900.

VASECTOMY has accomplished so little of permanent good that in spite of its harmlessness it has practically fallen into disuse.

CASTRATION, while admittedly curing a certain percentage of cases, is now less frequently practised because of its obvious æsthetic disadvantage, its surprisingly large mortality, and the great uncertainty of securing in any given case a benefit commensurate with its disadvantages.

BOTTINI'S OPERATION is still the most popular of the irrational methods for the relief of prostatic enlargement. While most of its ardent advocates still claim 40 to 50 per cent. of "cures," others are finding it too uncertain to be recommended. Frisch, formerly an enthusiastic advocate, now admits that he greatly overrated it, and that the remote results are far below the apparent immediate successes. Wossidlo, another zealous supporter, practically makes the same confession by his proposal to control the operative work through a new cystoscopic device.

The year's work has confirmed the conclusion formulated in this review for 1899,<sup>1</sup> that "the introduction of a finger into the bladder is essential to an intelligent operation; all measures which ignore this feature are blind experiments." And since the particular blind experiment known as the Bottini operation is accompanied by a mortality of 7 per cent. or more, it may be doubted whether the success sometimes achieved is not too dearly bought.

The one operation which, without permitting digital exploration of the vesical surface of the prostate, seems both safe and effectual is the "angioneurectomy" of Albarran.<sup>2</sup> The cases are as yet too few to warrant a conclusion, none having been reported the current year. Desnos,<sup>3</sup> however, mentions seven cases of prostatic enlargement with cystitis, in six of which the Heurteloup operation for varicocele caused a cure of the cystitis and ultimate marked decrease in the size of the prostate.

## UTRICLE.

This small but constant portion of the atrophied Müllerian duct in the human male has received but scant attention; in fact, until this year medical literature contained only two references to the clinical aspects of this organ. One of these emanated from Englisch,<sup>4</sup> who found in five out of seventy necropsies of new-born infants the utricle distended, sometimes rivalling the urinary bladder in size and offering a serious obstacle to urination. The other article was by myself;<sup>5</sup> it

<sup>1</sup> PROGRESSIVE MEDICINE, 1899, Vol. IV., p. 149.

<sup>2</sup> Ibid., p. 144.

<sup>3</sup> Annales d. Mal. d. Org. Gen.-Urinaire, January, 1900.

<sup>4</sup> Virchow-Hirsch, Jahresb., ii., 1873.

<sup>5</sup> Journal of the American Medical Association, April 21, 1894.

reviewed the comparative anatomy of the utricule, and related several cases of utricular abscess demonstrated by necropsy and by operation ; the probable frequency of infection from the deep urethra was mentioned ; the classical cases of Smith and Ralfe were reviewed, each called a cyst of the seminal vesicle by the reporter, who evidently did not comprehend the possibility of a cyst of the utricule, which each plainly was.

The last six years have furnished me many additional examples of utricular abscess, evacuated by pressure of the finger in the rectum, with or without the aid of a sound in the urethra. There can be little doubt that the condition commonly termed prostatic abscess and relieved by a gush of pus into the deep urethra is frequently an utricular abscess.

These matters acquire additional interest through the recent case of Kapsammer,<sup>1</sup> who removed from the utricule of a man, aged twenty-nine years, a stone as large as a goose-egg. The calculus was reached by a crescentic incision in the perineum and separation of rectum from bladder ; a piece of the sac was excised. Eighteen months later the return of symptoms and persistence of fistula led to a second operation ; by this the entire sac was removed excepting only the apex, which was not disturbed because of its evident coalescence with the peritoneum (moving with the respiratory movements).

The stone weighed when dried 162 grammes ; its exterior was calcium phosphate, its interior not examined. The sac had the histological structure of the vagina ; this, as well as the anatomical relations of the sac, prove it to be the utricule.

The most prominent clinical symptoms in this case had been frequent urination, occasional hæmaturia, fetid urine and semen.

This carefully observed case, together with the observations previously mentioned, should direct general attention to the utricule as a clinical factor in diseases of the male pelvic organs ; doubtless morbid states of the utricule have been confounded with those of the prostate, vesicles, and bladder in many cases beside those of Smith and Ralfe, above mentioned. The accessibility of the utricule to digital examination per rectum should make such mistakes infrequent when once the medical mind is alert as to its clinical possibilities.

## SYPHILIS.

Syphilis of the genito-urinary organs has been comparatively seldom recognized except in the testicle. Gummata of the kidney and prostate have been described in the literature ; syphilitic ulcers and cicatrices in

<sup>1</sup> Centralblatt f. Krankh. d. Harn. und Sexual Organe, January, 1900.



the bladder are mentioned by Virchow; but with what frequency it lodges in the urinary tract is still a matter of speculation. Two recent observations of Grinzow are of interest: The first concerned a woman whose cystitis had been unsuccessfully treated for years; an enlargement of the liver led to treatment for syphilis, whereupon the cystitis promptly ceased. In the second case a man infected six years earlier had cystitis for four years, in spite of varied treatment; a perforation of the hard palate led to treatment for syphilis, whereupon the cystitis ended abruptly.

**Justus' Test.** In 1896, Justus proclaimed, as the result of examination of 300 cases of syphilis in all stages, that an absolutely diagnostic sign of this infection is the sudden decrease in hæmoglobin which follows immediately the inunction or subcutaneous injection (but not the ingestion into the stomach) of a full dose of mercury.

This test has not been extensively employed. Jones<sup>1</sup> reviews the subject and relates his own observations in a series of cases. His conclusions are that it is a valuable though by no means infallible test; it often fails in latent cases, in early chancre, and the beginning of the secondary stage; and it occasionally gives a positive reaction in non-syphilitic cases. Thus, Cabot<sup>2</sup> observed a positive result in a case of non-syphilitic chlorosis.

**Syphilis without Primary Sore.** Marshall<sup>3</sup> reports as an instance of this a male patient who had gonorrhœa in January and a polymorphous secondary syphilide in March following. The conclusion seems irresistible that the gonorrhœa concealed an intra-urethral chancre, and that this case, like most of the others classified in this category, was one of syphilis with an undetected chancre. Doubtless many an observer since John Hunter has failed even to suspect the existence of an intra-urethral chancre, seeing in a purulent urethritis only a gonorrhœa.

**Digital Chancre.** Brandis<sup>4</sup> relates ten cases of chancre of the finger in physicians; all were severe infections, perhaps because the diagnosis was late.

**Syphilis and Marriage.** Jonathan Hutchinson says that the postponement of marriage to at least two years after infection would practically abolish hereditary syphilis, and that the dissemination of this knowledge throughout England has caused a marked decrease in the extent of inherited syphilis in that country.

This seems an exceedingly roseate view, in the light of frequent experiences to the contrary; indeed, it seems more probable that as time

<sup>1</sup> New York Medical Journal, April 7, 1900.

<sup>2</sup> Boston Medical and Surgical Journal, April 6, 1899.

<sup>3</sup> Lancet, May 20, 1899.

<sup>4</sup> Deutsche med. Wochenschr., 1898, No. 21.

alone never cures syphilis, no interval—unless that interval is employed in assiduous treatment of the infection—can be considered to justify marriage and procreation. Among recent observations as to the transmission of late syphilis are those of Lassar:<sup>1</sup> A woman married to a healthy man, seventeen years after she acquired a chancre, gave birth to a child which, when three weeks old, showed the usual signs of hereditary syphilis. Another patient, seven years after infection, was under treatment for an ulcerating gumma of the leg, when her healthy infant, six months old, developed a primary sclerosis of the labium majus.

De Melenes<sup>2</sup> describes hereditary syphilis, with fatal meningitis, in a child eighteen months old, whose mother had contracted the disease twenty-one years before its birth, and whose father was uninfected.

Granting that in some cases syphilis is absolutely eradicated, we cannot distinguish these from the far more numerous cases in which the infection is merely repressed for a time. The only rational advice is that the patient should take mercury and iodine one or two months in every year; this is essential to his own safety, and doubly so for the protection of possible children. Unless this is done, marriage and paternity are not justified, no matter what interval has elapsed since infection.

**Late Hereditary Syphilis.** Fournier<sup>3</sup> considers as trustworthy Lemonnier's observation that two brothers, aged twenty-seven and twenty-four years respectively, derived syphilis—from whose late manifestations, without history of primary sore, they were suffering—from a syphilitic father and grandfather.

**TREATMENT.** Fournier<sup>4</sup> considers ingestion the preferred method in ordinary cases, inunction for severe, and injection for the worst cases. He uses inunctions for old, tuberculous syphilides and tertiary visceral syphilis; injections of calomel for ulcerating gummata, persistent tongue lesions, and malignant cases generally. He considers mercury the agent for curing syphilis; iodine merely an effacer of its later manifestations.

Ward<sup>5</sup> advises mercury alone in primary and secondary syphilis; it should be pushed to the limit of toleration and continued in that quantity for two years. The iodides are advised against gummatous and severe secondary lesions.

Fournier repeats the old lesson that good nutrition is essential to the successful treatment of syphilis by presenting a case which had resisted heroic doses of mercury and iodine, but promptly yielded to somatose.

<sup>1</sup> *Dermatolog. Zeitschrift*, August, 1900.

<sup>2</sup> *Archiv f. Dermatol. und Syphilis*, April, 1900.

<sup>3</sup> *La Semaine Méd.*, August 15, 1900.

<sup>4</sup> *Annales de Dermatol. et de Syphilis*, May, 1899.

<sup>5</sup> *British Medical Journal*, October 21, 1899.

**Visceral Syphilis.** Friedländer<sup>1</sup> relates the successful removal of a gumma of the dura mater after failure of treatment by mercury and iodine.

Einhorn<sup>2</sup> describes two cases each of syphilitic gastric ulcer, syphilitic tumor of the stomach, and syphilitic stenosis of the pylorus. The two cases of ulcer were in women, and were naturally considered perforating round ulcers until the failure of medical and hygienic treatment and the history of syphilis led to the use of mercury and iodine, whereupon recovery promptly ensued.

The two cases of gastric tumor were in elderly patients, and presented some of the features of carcinoma. Syphilitic stenosis of the pylorus has not been recognized in the literature.

Fränkel<sup>3</sup> reports a case of gastro-intestinal syphilis in a man, aged forty-seven years, the autopsy disclosing thirteen ulcers in the stomach and thirty-one in the small intestine.

Flexner<sup>4</sup> adds another case of gastric syphilis, autopsy showing a perforating ulcer.

Dalgleish and others report cases of severe gastric and intestinal disease due to syphilis; Fournier says he has seen such from twenty to forty years after infection. They are readily relieved by mercurial inunctions and the internal administration of the iodides.

Legrain<sup>5</sup> reports three cases of syphilitic enlargement of the uterus simulating fibroid tumors, and suggests the possibility of confusion between the two in other cases.

Grinzow describes two cases of refractory cystitis in subjects of syphilis unimproved by years of other treatment, but promptly cured by the usual treatment for syphilis.

Fournier<sup>6</sup> discusses certain manifestations of syphilis in the nervous system, especially in women. Prominent among these are persistent headache, insomnia, asthenia and neuralgia; the latter is frequent in the sciatic and fifth nerves, notably as supra-orbital neuralgias.

Rodbiceck<sup>7</sup> asserts that interstitial keratitis when due to acquired syphilis is unilateral, when caused by hereditary syphilis, bilateral; the latter is not healed by specific remedies.

Diez<sup>8</sup> traced more than half of his cases of parenchymatous keratitis to tuberculosis and only 34 per cent. to hereditary syphilis

<sup>1</sup> Wiener klin. Wochenschr., 1898, No. 4.

<sup>2</sup> Philadelphia Medical Journal, February 3, 1900.

<sup>3</sup> Virchow's Archiv, Bd. clv., Heft 3.

<sup>4</sup> American Journal of the Medical Sciences, October, 1898.

<sup>5</sup> Annales des Mal. des Organes Gen.-Urinaire, April, 1898.

<sup>6</sup> Journal de Médecine, April, 10, 1899.

<sup>7</sup> Wiener klin. Rundschau, 1899, No. 35.

<sup>8</sup> Zeitschrift f. Augenheilkunde, vol. i., No. 5.

The diagnosis of visceral syphilis is of necessity dependent in part upon the effect produced by mercury and iodine, and this fact renders such diagnosis at times uncertain; for not only do some lesions caused by syphilis resist these remedies as usually administered, but there are also other morbid conditions which yield readily to the same remedies. Prominent among these is actinomycosis, which, like syphilis, may attack the lung, liver, intestinal canal, and other viscera; and Bevan has noted the curative effect of the iodides upon one of Hyde's cases of blastomycetic dermatitis. It must be admitted, therefore, that the therapeutic success of these remedies does not warrant a diagnosis of syphilis as the cause of a visceral lesion; yet until the infecting agent shall be discovered and identified we must be content with the present incomplete data.

Belfield<sup>1</sup> reports a case in which a breast was removed for ostensible carcinoma; a year later the remaining breast exhibited similar signs. Persistent headache caused a suspicion of syphilis and the administration of iodides, whereupon the breast lesion disappeared. The woman had contracted syphilis twenty years prior to this time. This and a second case mentioned in the same article illustrate the possibility of mistaking syphiloma for carcinoma of the breast—an error which has perhaps led to many unnecessary operations.

Janeway<sup>2</sup> calls attention to the fact that secondary syphilis may be accompanied by a continued fever, and that this symptom may, in the absence of accessible local lesions, lead to a mistaken diagnosis of visceral tuberculosis. He narrates several instances in which this mistake was made.

Pellicke<sup>3</sup> asserts that syphilitic disease of the joints may be accompanied by fever and by local swelling and tenderness, leading to a mistaken diagnosis of acute rheumatism or tuberculosis.

The impossibility of knowing when, if ever, the syphilitic virus is eradicated from a given patient; the lack of a histological element distinctive of syphilis; the simulation of many other diseases, notably tuberculosis, by the syphilitic infection—all these have led me to impress upon every patient whom I treat for syphilis the wisdom of informing every physician who may be in the future consulted that the patient contracted syphilis at such a time. This and the injunction to take mercury and iodine January and July of each year of his life are emphasized to the utmost. A large part of the literature of syphilis would be unwritten could these two behests be generally preached and practised.

<sup>1</sup> Chicago Medical Recorder, April, 1900.

<sup>2</sup> American Journal of the Medical Sciences, September, 1899.

<sup>3</sup> Berliner klin. Wochenschr., 1898, Nos. 4 and 5.

# FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE EXTREMITIES, AND ORTHOPEDICS.

BY JOSEPH C. BLOODGOOD, M.D.

## SURGICAL SHOCK.

**Cocainization of Large Nerve Trunks to Block Afferent Impulses and Prevent Shock.** In *PROGRESSIVE MEDICINE* for December, 1899, in my review of Crile's work on experimental shock, I wrote (p. 155): "Clinically, we seldom observe sufficient depression after the division of large nerve trunks to influence us to make use of cocaine; however, in amputations during shock this might be tried; every factor, no matter how small, which aids in lessening the shock is of great value."

Cushing,<sup>1</sup> in his review of the same work, writes: "Possibly, from a practical stand-point, the most valuable suggestions from Dr. Crile's work originate in the results from his observations upon the 'blocking' effect of the preliminary local administration of cocaine as a preventive measure toward shock in anticipation of those peripheral manipulations which ordinarily have a marked depressor effect. This is most strikingly shown in one of the composite charts (near page 127; these charts, unfortunately, are not numbered) which illustrates the great fall in blood-pressure that ordinarily follows upon manipulations of the larynx, and in the inhibitory effect of preliminary cocainization of the mucosa upon this fall."

Cushing was probably influenced to write so strongly on this point from two of his own observations, which he has communicated to me. In both cases the operation was a complete exarticulation of the upper extremity with the scapula for sarcoma of the humerus, involving the joint. In the first case, a woman, the pulse chart kept during the operation every five minutes showed no marked change until during and after the division of the brachial plexus; at this stage of the operation the pulse-rate became suddenly more rapid, and the symptoms of distinct shock were observed; during the operation there had been practically no loss of blood. The patient recovered. At the second

<sup>1</sup> Johns Hopkins Hospital Bulletin, March, 1900, vol. xi., p. 73.

operation these nerves were cocaineized with a 1 per cent. cocaine solution before division, and no change in the pulse and general condition of the patient was noted, and at the end of the operation the general condition of the patient was a marked contrast to that observed in the first. This patient also recovered. These two operations, with Crile's experimental results, I believe, are sufficient to establish as a routine procedure the cocaineization of large nerve trunks as a preliminary procedure to their division, whether the patient is in a condition of shock or not at the time of operation.

Mitchell<sup>1</sup> reports an interesting case in which the relation of shock to nerve injuries is well illustrated. The patient (I observed, with Dr. Mitchell, Case II. of the report) was admitted to the hospital in a condition of extreme shock; the injury was an extensive crush of the upper extremity, and, as Mitchell writes, "the skin of the arm was torn from the shoulder down, just as you tear out the sleeve of a coat." Although the pulse-rate was but 80, there was low tension and very little volume (a good illustration of the fact which we frequently observe—no marked acceleration of the pulse-rate in extreme conditions of shock, especially if there has not been great loss of blood); the respirations were 40, and the temperature 97.5° F. per rectum. The patient was placed at once in bed in the accident-room and the foot of the bed elevated; 600 c.c. of a 0.6 per cent. salt solution (temperature about 101° F.) were infused slowly in the subcutaneous tissue between the breast and the pectoral muscle; morphine, gr.  $\frac{1}{8}$  (on account of pain and restlessness), was given hypodermatically; a hot enema of coffee (4 ounces) and salt solution (8 ounces) was retained after introduction high up in the rectum. The patient was admitted at 6.30 P.M., and up to 10 P.M. he was kept in the same position, the injured extremity being wrapped in sterilized gauze. During these three and a half hours a gradual improvement was noted in the pulse tension and volume, and the respiration-rate became slower. About this time, coincident with the onset of considerable oozing from the injured arm, the condition of the patient rapidly became worse; the pulse and respiration-rate increased, associated with marked restlessness. It is to be noted that from the time of admission up to this moment there had been no oozing from the injured arm, and as far as could be ascertained from those who had been with him from the time of the injury up to his admission to the hospital—a period of perhaps an hour and a half—there had been very little loss of blood; surely not sufficient to explain the extreme condition of shock, which was without doubt due to the great tearing and crushing of the arm, especially about the brachial plexus in the axilla. At 11 P.M. it

<sup>1</sup> Johns Hopkins Hospital Bulletin, January, 1900, vol. xi., p. 32.

was considered best to remove the arm, because the signs of reaction from shock had ceased. Before the administration of the ether the patient was given a second salt infusion, one-thirtieth grain of strychnine, and was placed in a position of greater elevation and the legs tightly bandaged. The anæsthetic time was but ten minutes; the amount of ether not more than 50 grammes. The operation consisted of a very rapid amputation of the arm, just below the shoulder. Just before Dr. Mitchell cut the large nerves I could distinctly feel the radial pulse; after the division of these nerves, which took but a minute or two, the radial pulse disappeared and could not be felt again for ten minutes. At this time the heart sounds could scarcely be heard. The amputation took but five or six minutes, with practically no loss of blood. At the moment of this collapse a third infusion was given and three hypodermatic injections of one-thirtieth grain of strychnine in rapid succession. Associated with this, and about ten minutes after the division of the nerves, the radial pulse was again felt and the heart sounds more clearly distinguished. For the next twelve hours the condition of the patient was critical; the temperature rose to 103.6° F., and he became delirious; then he slowly became quiet, and the recovery from shock was rapid; there was no infection of the wound, which had been left open. The coincidence of the apparently almost fatal collapse during the division of the nerves is an observation in support of Crile's experimental results and Cushing's observation. In Mitchell's case, however, we must consider that the element of the depressing effect of the anæsthetic was also present. In this case it would have been a very simple procedure to have cocaineized the nerves.

**Research into the Cause of Collapse or Death from Blows upon the Lower Chest and the Epigastrium.** Under this title Crile<sup>1</sup> contributes another experimental research on surgical shock. In all the experiments the animals were reduced to full surgical anæsthesia by ether and killed before recovery. Crile states that "this research was suggested by a number of cases of collapse and even death following blows delivered upon the chest, more especially over the lower portion of the left anterior chest-wall and upon the so-called 'pit of the stomach.' In the history of these cases it is usually stated that such results instantly followed the application of the violence, and that if death did not immediately follow, recovery took place. The so-called 'short rib' and 'solar plexus' blows, well known in pugilistic encounters, are examples." It is important to observe that Crile states that if death did not immediately follow, recovery took place. As a matter of fact, we seldom observe death from such injuries alone, although there seems to

<sup>1</sup> Philadelphia Medical Journal, March 31, 1900, vol. v., p. 744.

be no question from clinical observations that a blow on the "pit of the stomach" is usually associated with marked collapse; but, as I wrote in *PROGRESSIVE MEDICINE* for December, 1899, such a condition of shock not associated with loss of blood or injury to the brain or spinal cord, if not followed at once by death, never produces the same mortality as when the same condition is associated with hemorrhage.

Crile makes the following summary after fifteen experiments: "No amount of injury inflicted upon the solar plexus, either directly or indirectly, was capable of causing any inhibitory action upon the heart, and in no way did such injury contribute to the immediate death or collapse referred to; but the effect this manipulation did have was to produce a vasodilation of the 'splanchnic area,' thereby causing a gradual decline in the blood-pressure.

"In experiments in which the abdomen was opened and the diaphragm protected from indirect violence, blows upon the stomach alone produced but little effect upon the blood-pressure or the respiration.

"In other experiments in which the diaphragm was not protected from indirect violence transmitted through the stomach or other viscera, blows delivered on the pit of the stomach, especially when the stomach was distended, produced sometimes a momentary staggering fall in the blood-pressure. In some cases the blood-pressure remained at a lower level and described a very irregular curve, then finally regained the height of the control.

"Pressure suddenly applied, or blows directly upon the diaphragm within the cardiac zone, produced usually a very marked drop in the blood-pressure. In some cases but a single intermission of the heart-beat was produced; in others the blood-pressure suffered a great fall, and slowly and with great irregularity of action regained the lost pressure. Even carefully pressing with the hand upward against the diaphragm so as to produce by such pressure an interference with the freest movement of the apex caused a very great cardiac irregularity and an irregular blood-pressure.

"Blows delivered upon the lower chest, especially over the cardiac area, produced various results. In one case the heart was instantly arrested from the effect of a smart, but not heavy, blow from a small hammer over the cardiac area, and death at once ensued. Respiratory action was as suddenly arrested. The most common result was a very great drop in the blood-pressure—a collapse; then, after a variable time, the heart would regain its normal action and the lost blood-pressure recovered.

"The effects, as nearly as observations would permit deductions, varied in different dogs, the blow being delivered with about the same force, with the same instrument, and, as nearly as may be, at the same



point of application. On the whole, it may be said that the more nearly the blows were delivered over the centre of the area of the cardiac dulness the greater the effect. Blows delivered upon the naked heart *in situ* produced like results, though more profound.

"The evidence thus far offered tends to show that the solar plexus may be disregarded as a factor, and that the cause of the striking phenomena is the mechanical effect of violence upon either the heart muscle itself or upon its nerve mechanism. If the vagi contributed to the collapse it was either by a direct or a reflex inhibition—interpreting direct inhibition as that due to an excitation of the trunk of the vagus or its cardiac branches, and the reflex as afferent impulses sent up to the centre in the medulla from irritation of some branch of the vagus—*e. g.*, the superior laryngeal. In the animals in which both vagi had been previously severed, when the foregoing experiments, blows, etc., were repeated, like results were produced. The collapse, then, in these cases, could not be due to reflex inhibition, because the path by which the afferent impulses reach the heart had been severed.

"In the experiments in which atropine in sufficient dosage to paralyze the terminals of the vagi in the heart was given, and this dosage was proved by applying a faradic current from a Du Bois-Reymond apparatus to the vagi while the secondary coil was lapping the primary by half, upon repeating the foregoing experiments like results were obtained, though as nearly as could be estimated the collapse was not so prolonged as before.

"Collapse or death may be caused wholly independently of the vagi, though the vagi probably slightly contribute to the result.

"Finally, collapse or death from violence applied upon the lower chest or abdomen are due mainly to the loss of rhythmic contractions from the mechanical irritation of such violence on the heart muscle itself. There is evidence tending to show that the vagal terminal mechanism in and near the heart may contribute to the result, but in a minor degree.

"The practical deductions are sufficiently obvious and need not be repeated."

The collapse or shock associated with contusion of the abdomen is frequently observed clinically. Recently, Mr. J. B. McCallum, of the graduating class of the Johns Hopkins Medical School, made a very careful study and *résumé* of thirty-four cases. We must exclude from these cases thirteen (injury to solid viscera with hemorrhage, 4; rupture of intestine, 3; of bladder, 3; of urethra, 3). In the remaining twenty-one cases there were distinct symptoms of shock unassociated with any hemorrhage. In eleven cases it is to be noted that shock was more intense and more common in those cases in which the contusion was

at or near the pit of the stomach. The study of these eleven cases teaches us that it is very difficult to differentiate the cases suffering from shock pure and simple due to the contusion from those in which there is in addition hemorrhage from rupture of some solid viscera or beginning peritonitis from rupture of the stomach or the intestine. Such a differential diagnosis, however, is of the greatest importance, because in case of hemorrhage or peritonitis from rupture, unless the operation is performed within a few hours a recovery cannot be expected. In cases of extreme shock or collapse from contusion over the abdomen this study clearly indicated that an exploratory laparotomy should be performed at once, because it is impossible to differentiate the cases associated with hemorrhage.

Such an exploratory laparotomy, which can be done under cocaine, will give the patients in which there is hemorrhage the only opportunity for recovery, while in the other cases the mortality is not increased by the operative procedure. In those cases of shock due to contusion, with no other injury, and in which the condition is not an extreme one, positive symptoms of reaction usually take place in three or four hours or less; while if there is a rupture of the intestine the local abdominal symptoms of beginning peritonitis rapidly supervene on the symptoms of shock. This observation clearly demonstrates that in a case of contusion of the abdomen with moderate symptoms of shock an exploratory laparotomy should be performed if the signs of reaction do not take place within three or four hours. The prognosis of cases of shock associated with contusion of the abdomen in which there is no injury of the solid or the hollow viscera is always good, and even in those few cases where we have performed exploratory laparotomy, although the condition was temporarily made worse by the general anæsthetic, the patients have rapidly recovered. Laparotomy under cocaine anæsthesia should, however, if possible, be done. Our few observations have demonstrated that it does not increase the severity of the shock.

Although Crile's experimental work just quoted is of great interest, practically we need experiments or observations of an almost opposite character—that is, given a patient or an animal suffering from a condition of shock due to trauma alone or trauma and hemorrhage. What is the effect on this condition of a general anæsthetic which might be necessary to allow the operative interference for the relief of the injury? As yet we have no experimental evidence in this direction. Clinically, a general anæsthetic, chloroform more particularly, is a distinct depressing agent in these conditions of shock, especially in those associated with the loss of blood. In many cases, however, the danger of delay is greater than the danger from the anæsthetic. Unquestionably, however,

if the operation can be performed under local cocaine anæsthesia it should be done, and every surgeon should school himself thoroughly in the use and possibilities of local anæsthesia.

Remedi,<sup>1</sup> from his experiments on animals, comes to a different conclusion from Crile. He emphatically states that the chief depressive agent on the blood-pressure is due to the general anæsthetic, and that there is little effect on the blood-pressure from opening of the various body cavities or handling with different degrees of trauma the various tissues and organs.

**Literature on Shock.** During the last two years one finds few publications on shock pure and simple, except in the articles on transfusion, which will be considered later. In *Jahresberichte über die Fortschritte auf dem gebiete der Chirurgie*, Hildebrand, for 1898-1899, I find but two references to the subject of shock in a complete consideration of the literature of 1898 and 1899. In the present year there are a few communications, chiefly by English and American surgeons, but in a careful reading of them all I can find little which has not already been discussed, either in an article in *PROGRESSIVE MEDICINE* for December, 1899, or the present one.

**The Value of Repeated Small Hypodermatic Doses of Strychnine in the Treatment of Shock.** The majority of writers agree with Crile<sup>2</sup> that strychnine is an important remedy. J. Basil Hall<sup>3</sup> reports a few cases and advocates the use of strychnine. Hall writes: "I can only say that after a thoroughly extensive trial of strychnine in cases of severe shock I have yet to see a case that displayed any symptoms of overdose, and I am confident that the drug has proved of great service when freely given." He reports a few cases in detail. Moyhihn,<sup>4</sup> in an article entitled "On the Prevention and Anticipation of Shock in Surgical Operation," advocates the use of strychnine, and refers to the statement of Müller that patients in the condition of shock have great tolerance to the drug. Unquestionably strychnine is an important drug and should be given freely.

The use of hypodermatic injections in the treatment of both traumatic and post-operative shock should not be an indiscriminate one. In traumatic shock, if the patient when first seen is in great collapse, one, of course, should give hypodermatics of strychnine and atropine at once, in order to help maintain a sufficient vasomotor tone necessary to preserve life until fluid is introduced into the circulation by transfusion. In such an extremely critical condition the high elevation of the lower extremities of the patient and the application of external heat are always

<sup>1</sup> Centralblatt f. Chirurgie, 1900, vol. xxvii., No. 4.

<sup>2</sup> Quoted in *PROGRESSIVE MEDICINE* for December, 1899.

<sup>3</sup> British Medical Journal, November 25, 1899.

<sup>4</sup> Ibid.

important adjuncts. If, however, the condition of collapse is not extreme it is better to delay the use of the hypodermatic injections of strychnine and atropine until a few hours later, when, if a general anæsthetic is necessary for some operative interference, these drugs will be of better service at a more critical time. In addition, unless such hypodermatic medication is urgently indicated, their administration will mask the real condition of the patient and perhaps hinder the surgeon in making a correct estimation of the condition in regard to operative interference.

During operations I am firmly convinced that one should delay as long as possible the administration of strychnine or atropine or any other stimulant except, perhaps, transfusion or rectal enemata. If the patient's condition is sufficiently critical to demand these drugs the anæsthetic should be discontinued and the operation finished as rapidly as possible. For this reason they should not be administered until the operator has decided that the operation should be finished and the anæsthetic removed. All authorities agree that digitalis is of no value, as it takes too long to act. The administration, by inhalation, of aromatic spirits of ammonia, or any form of ammonia, is unquestionably a good stimulation to carry a patient over a few minutes during a slight syncope. Many questions in regard to both traumatic and post-operative shock are still unsettled, and there is excellent opportunity both for experimental and clinical work.

### EXAMINATION OF THE BLOOD IN SURGICAL CASES.

**The Blood Examination in Traumatic Shock.** Cabot<sup>1</sup> writes: "Often one hears the question discussed in any accident-room in any hospital whether to operate at once or wait until the patient has got over the shock. The question is not often asked, far less answered, whether the shock is simple or largely anæmia (cerebral or general) from loss of blood, or whether it is of nervous origin—*i. e.*, due to concussion or compression. The right decision of this question is of great importance; for if the shock means anæmia, transfusion may be indicated, while in a condition of cerebral concussion or compression, transfusion will probably do harm. [Authorities do not agree with Cabot. Transfusion is not contraindicated, see p. 108.] An examination of blood enables us in certain cases to decide such a question—that is, if the number of red cells is considerably diminished (3,500,000 or less) and the patient is known not to have been previously anæmic, the shock probably means

<sup>1</sup> Clinical Examination of the Blood. Wm. Wood & Co., New York, 1898. International Text-book of Surgery, Warren and Gould, 1900, vol. i., p. 81.

hemorrhage." "The blood-count may enable us to gauge approximately the amount of hemorrhage. Here it should be remembered, however, that immediately after hemorrhage the count may be normal, since only the amount and not the quality of the blood is affected. Within a few hours, however, fluid is absorbed from the tissues into the vessels, and then an anæmia will be indicated by the blood-count." "An internal or cerebral hemorrhage, as in obstetric cases, extra-uterine pregnancy, ruptured aneurism, laceration of the spleen, kidney, and liver, etc., can sometimes be diagnosed by the blood examination."

McLean,<sup>1</sup> in his article entitled "Examination of the Blood in Surgical Diseases," practically adds nothing new to Cabot's statement with regard to the blood examination in shock. In his table of twenty-two counts in various conditions there are no cases, however, illustrating this point. I can find nothing further in recent literature. Cabot in his book has recorded but very few observations, and we have had but few observations in Prof. Halsted's clinic in regard to this point. In Mitchell's case (see p. 92) at the time of the operation, about five hours after the accident, the blood-count was: red corpuscles, 5,000,000; white, 23,000; hæmoglobin, 70 per cent. Thirty-six hours later the blood-count was: red corpuscles, 3,000,000; white, 12,000; hæmoglobin, 50 per cent. In this case the element of hemorrhage in the shock was not great.

Cabot states the blood-count would not show the presence of secondary anæmia, at least for five or six hours; but one should not like to wait that long before treating the patient for shock. As will be discussed later, transfusion is indicated not only in shock from loss of blood, but from shock pure and simple, although, of course, in the former instance it is of the greater value. However, we usually wait from four to six hours before instituting any necessary operative interference, and I believe in every case a blood-count should be made. The presence of a marked anæmia would be additional positive indication to diminish the amount of the anæsthetic as much as possible and to shorten the time of the operation. There have not been sufficient observations to draw any conclusion whether in contusion of the abdomen, with or without a rupture of solid viscera and internal hemorrhage, that the blood-count would help us at a sufficiently early date in hemorrhage to save the patient's life. As a rule, in such cases it is a matter of much less than six hours, and any operative interference to save the patient's life must be instituted very quickly after the injury.

**Leucocytosis Following Hemorrhage.** Cabot<sup>2</sup> states in his book that "within an hour after a large hemorrhage we find commonly a considerable increase in the leucocytes (16,000 to 18,000)." I have observed

<sup>1</sup> Medical News, December, 1899, vol. lxxv., p. 713.

<sup>2</sup> Loc. cit.

this in a number of traumatic cases, but as yet have not had sufficient observations to indicate whether the increased number of leucocytes has any relation to the amount of hemorrhage. I have yet to observe a case of shock pure and simple in regard to leucocytosis.

These observations, although meagre, are of great importance, and in every case of traumatism associated with shock a careful and complete blood-count should be made immediately after the patient is seen and four or five or six hours later. A collection of such careful counts may be found to be of great value.

**The Importance of Blood Examinations in Reference to General Anæsthesia and Operative Procedures.** Cabot<sup>1</sup> quotes Mikulicz in the following statement: "The examination of the blood throws so much light on the condition of surgical patients as to make it a useful rule that every patient's hæmoglobin should be tested once a week. This is done partly to watch the progress of the patient after bloody operations and partly to ascertain whether it is advisable to operate upon patients already anæmic. Mikulicz makes it a rule never to operate on a patient whose hæmoglobin is under 30 per cent. This gives him a standard up to which patients must be brought by treatment before he will subject them to further loss of blood."

Hamilton Fish<sup>2</sup> has an excellent article in regard to this important fact. He believes many deaths attributed to anæsthesia or slight loss of blood during operation are due to the presence of anæmia, and had such patients been prepared previous to operation, and had the surgeon delayed until the blood-count had increased, death would not have taken place. He firmly believes that the blood-count is a good index for operative interference. He states: "In individuals whose blood presents a hæmoglobin percentage of 50 or less the anæsthetic vapor produces an increased pathological condition by a forced abstraction of oxygen from the tissue ill-conditioned to part with it." Hence, it is not surprising that these individuals show quickly the signs of collapse. A safe rule to follow is never to produce a general anæsthetization in an individual whose blood shows a hæmoglobin percentage of less than 50. Chloroform and ether seemed to have a similar action. Fish seems to think that perhaps chloroform is least dangerous. In conclusion he states: "Safety in anæsthesia and operative procedure is dependent, first, upon the hæmoglobin percentage over and above that required for its normal duties; second, a normal or increased number of polynuclear neutrophiles. Under these conditions anæsthesia may be produced and operative procedures conducted with the assurance of perfect safety. The statements of Mikulicz, Cabot, and Fish are important ones, although

<sup>1</sup> Loc. cit.

<sup>2</sup> Annals of Surgery, 1899, vol. xxx., p. 79.

they do not give any large number of specific observations to conclusively demonstrate the point. In my own experience in a few cases in which it has been confirmed by a blood examination, both before and after operation, a marked condition of anæmia has always been associated with a more or less post-operative shock, so much so that we are in the habit, if possible, of postponing operations on anæmic patients until proper treatment has partly or completely restored the blood to its normal condition. My most important and interesting observation was the following (surgical number 9722): A young woman, aged about twenty-two years, suffering with a chronic osteomyelitis of the upper end of the femur, involving the hip-joint. The disease had been present some two years; there were a number of sinuses, and the patient's general condition was not very good. However, from an ordinary examination, one would not have considered the patient very anæmic. The blood-count, however, showed 3,076,000 red corpuscles, 9600 white, and hæmoglobin 54 per cent. The operation was rather a tedious one, but there was practically no loss of blood. The anæsthetic was ether. The operation was a long one, because the bone in places was very eburnated and a good deal of chiselling was required, and there was so much scar-tissue that to perform the operation about the hip bloodlessly it had to be performed slowly and carefully. The pulse, however, at the beginning of the operation was 90. The anæsthetic-chart records the pulse-rate every five minutes, and shows that the pulse for the first hour and thirty minutes was between 90 and 110. About this time (the anæsthetic was well taken) the patient suddenly became pale and the pulse very weak; the rate rapidly rose to 160. The ether was at once removed; the operation had been about completed. There was no cyanosis. The condition of collapse came on suddenly, and for a half or three-quarters of an hour the patient's condition was critical. One could hardly feel the radial pulse; it was very rapid; the heart sounds were weak; the lips were pale; the breathing was shallow. It was about as an extreme condition of collapse as I ever wish to observe on the operating-table in a patient whose condition at the beginning of the operation was apparently good. I felt, however, that in view of the fact that the loss of blood during the operation had been insignificant that the prognosis was good. The moment this condition was noted the anæsthetic was removed; the foot of the table was elevated so that the body lay at an angle of at least 45 degrees, and strychnine and atropine were given hypodermatically and a subcutaneous infusion of salt solution. At the end of about four hours the patient's condition was sufficiently improved to allow her removal to the ward. A glance at the temperature-chart shows that the tachycardia lasted for twelve days, and the pulse-rate for at least

three weeks was higher than normal. Although the hemorrhage during the operation without doubt was insignificant, the hæmoglobin count fell in twenty-four hours to 30 per cent., and the red corpuscles from 3,000,000 to 2,000,000. Twenty-four hours later the red corpuscles were 3,700,000, about similar to the count before operation. The count varied from day to day from 2,800,000 to 3,900,000. The hæmoglobin at the end of five days rose to 40 per cent.; at the end of fifteen days to 43 per cent.; white and red corpuscles about the same. The hæmoglobin did not reach 51 per cent. until eight weeks. At this time the red corpuscles were 4,000,500. About three months later a second operation was performed. At this time the hæmoglobin was 54 per cent.; red corpuscles, 4,500,000. The operation lasted but thirty-five minutes. The pulse, which at the beginning was 100, rose within twenty-five minutes to 140. A short time after the anæsthetic was removed it fell to its normal rate, and no tachycardia followed the operation. At a third operation, done some months later, during which ether was given for at least forty-five minutes, and at which time the blood-count was practically normal, no change in the pulse was noted during or after operation. This observation has convinced me that surgeons should follow Mikulicz's rule, and when it is absolutely necessary to operate on anæmic patients the anæsthetic should, if possible, be a local one, and if a general anæsthetic is necessary, the time should be shortened. As far as the loss of blood is concerned during the operation with modern methods, this can be so controlled as hardly to be considered a factor. Unquestionably, observations show that in a condition of anæmia, especially when the hæmoglobin percentage is low, the general anæsthetic is a distinct depressant, and if prolonged may be followed by serious or even fatal collapse. These observations demonstrate that the work of the surgical interne is increased. Now he must make not only a careful physical examination and a urine examination, but a careful and complete blood-count before every operative interference, especially if a general anæsthetic is used.

**The Importance of the Leucocyte Count as an Aid to Differential Diagnosis in Various Surgical Conditions.** This subject I will consider more carefully in *PROGRESSIVE MEDICINE* for December, 1901. In the meantime I would refer those interested in the subject to Cabot's third edition of his book (1898), which unquestionably is the best in English. One will find recent articles by Durham,<sup>1</sup> a discussion in the *Transactions of the New York Surgical Society*,<sup>2</sup> J. C. Hubbard,<sup>3</sup> and H. Stuart McLean.<sup>4</sup>

<sup>1</sup> *Annals of Surgery*, June, 1900, vol. xxxi.

<sup>2</sup> *Ibid.*, July, 1900, vol xxxii.

<sup>3</sup> *Boston Medical and Surgical Journal*, April 19, 1900.

<sup>4</sup> *Medical News*, 1897, vol. lxxv.



**GELATIN.**

**The Hæmostatic Use of Gelatin.** The demonstration by Dastre and Floresco that gelatin increases the coagulability of the blood is an important addition to surgical therapeutics. Although not introduced until February, 1896, the literature on the subject is rich. Dr. Alfred Bass,<sup>1</sup> of Vienna, has given us an excellent collective review of the literature, with forty references. J. B. Nichols,<sup>2</sup> of Washington, has also collected the literature, but somewhat less extensively, and given us a very clear *résumé* of the subject.

**The Local Use of Gelatin.** Unquestionably when suitable the coagulating power of gelatin is best when applied locally; this was first demonstrated by Paul Carnot.<sup>3</sup> As Nichols<sup>4</sup> writes, the solution of gelatin for the purpose of arresting hemorrhage locally should consist of 5 to 10 per cent. of gelatin with 0.6 to 1 per cent. of calcium chloride or sodium chloride in 100 parts of water. This should be sterilized by the ordinary fractional method for fifteen minutes on two or three successive days, and it is important to avoid a temperature in excess of 100° C. This 10 per cent. gelatin is the ordinary culture medium used in the bacteriological laboratory, except that the peptone is not added. This is an important thing to remember, because when peptone is present it counteracts the coagulative action of gelatin. Some authorities advise for the local application to add 0.1 per cent. of bichloride of mercury or a little glycerin. These antiseptics, of course, should not be added when the gelatin is injected subcutaneously. The local use of gelatin has been used with good results in many conditions where it is possible from the anatomical situation to apply it directly on a cotton pledget, using in addition, of course, all other surgical means of checking hemorrhage. Their results in epistaxis have been excellent, although one should never neglect to plug most completely the anterior and posterior nares. There are a number of cases reported of excellent results in hæmophilia with bleeding from different external areas. In hemorrhage from the gastro-intestinal tract, of course we can use the local action only in the stomach and in the rectum. The results in gastric hemorrhages have not been as good as in other parts; due, perhaps, to the action of the gastric juice. The results, however, are sufficient to indicate that in hemorrhage from the stomach both the local and the subcutaneous injection should be used. Good results have been obtained in hemorrhage from the bladder and in

<sup>1</sup> Centralbl. f. die Grenzgebiete de Med. u. Chir., March 15, 1900, Bd. iii., No. 6, p. 209.

<sup>2</sup> Medical News, New York, 1899, vol. lxxv., p. 705.

<sup>3</sup> Loc. cit.

<sup>4</sup> Loc. cit.

uterine hemorrhage. I am surprised to find that neither Nichols nor Bass, in their study of the literature, have mentioned any cases in which gelatin was used in the hemorrhage associated with jaundice. In such instances I should think the value of gelatin should be tested, for here we know the coagulability of the blood is lowered. It would seem that it would be a good plan to use the gelatin first subcutaneously before operation, repeat it again after operation, and if there is oozing from the wound to apply the gelatin locally to the oozing surfaces. The coagulability of the blood of the jaundiced patient should be tested before operation, then subcutaneous injections of gelatin should be given, and the coagulability tested again. If the power of coagulation of the blood was greatly reduced and we found that the injection of gelatin increased this power, the contraindication to operation on account of hemorrhage would be lessened and we would feel that we had the means of checking it if it did occur after the operation. Clinically, we know that only a small percentage of jaundice cases bleed seriously after operation; but there have been a sufficient number of deaths after operation, due entirely to hemorrhage, to make the surgeon welcome the use of gelatin if future work demonstrates its value.

**The Internal Use of Gelatin.** As Nichols writes: "In cases where the seat of hemorrhage is not directly accessible the hæmostatic action of gelatin can be obtained by introducing it into the circulation." This should be done subcutaneously, as intravenous injections are dangerous. Gelatin by the mouth or per rectum is not absorbed as rapidly as when injected subcutaneously, although it has been demonstrated that per rectum it has some power. Experience has demonstrated that the nearer to the point of hemorrhage one can inject the gelatin the better the result. Bass records no bad after-effects or dangers after the subcutaneous injection of gelatin. Nichols records two deaths—one by Boinet,<sup>1</sup> in a patient suffering from an aneurism; the clot which formed in the sac pressed upon the pulmonary artery, restricting the blood-supply to the lungs, and pulmonary tuberculosis developed. Although Boinet attributed the death of his patient to the injection of gelatin, Nichols very correctly questions whether the result was even remotely due to the subcutaneous injection of gelatin. A second case was that of Barth (no reference given). His patient was a woman, suffering with an aneurism of the arch of the aorta, to whom thirteen subcutaneous injections of gelatin had been given. The last injection was a 30 c.cm. of a 2 per cent. solution. A few days later the patient was suddenly seized with dyspnoea and syncope, which were rapidly followed by cyanosis, collapse, and death. At the autopsy the aneurismal sac was

<sup>1</sup> *Revue de Méd.*, Paris, 1896, p. 509.

filled with dark clots, which extended beyond the sac into the left internal carotid artery. The two bad results were, therefore, in aneurism, and it is a danger common to any method which hopes to cure the aneurism by coagulation of the blood in the sac.

**Solution of Gelatin for Internal Use.** Lancereaux and Paulesco, from their experience in the treatment of aneurism with subcutaneous injections of gelatin, recommend a 2 per cent. sterilized aqueous solution of gelatin with 0.7 per cent. of sodium chloride. Two hundred c.c. of this solution may be injected at each sitting, and the infusion may be repeated at intervals of four to eight days. Huchard used the following solution: Gelatin, 7 parts; sodium chloride, 10 parts; water, 1000 parts; the amount to be injected, 50 c.cm. This solution was used by Huchard in a case of hæmoptysis from tuberculosis of the lungs. On the whole, the solution recommended by Lancereaux and Paulesco seems to be best for subcutaneous use. It is even of greater importance, when used subcutaneously, that the solution should be most carefully sterilized. This is not difficult, for one should always allow the solution to stand three or four days after the last fractional sterilization. The least cloudiness of the gelatin solution would indicate its infection. Ordinarily the subcutaneous injection of the gelatin solution causes no disagreeable reaction or consequences. De Guy has noted fever with slight rigors and insomnia, or there may be local pain and tenderness, diffuse redness or induration about the seat of injection. I should judge with the proper antiseptic precautions and with sterile gelatin solutions the dangers of infection from the subcutaneous injection would be very slight. One must be careful not to use too strong solution or too large or frequent injections, as one might increase the coagulability of the blood to too great a degree. Any form of internal or external hemorrhage associated with hæmophilia or not associated with it should be treated with gelatin externally, if possible, and subcutaneously when other means have failed to check the hemorrhage. There are too many successful cases in the literature to allow the surgeon to neglect the therapeutic use of gelatin. In surgery, however, the majority of cases of hemorrhage can be checked by ordinary means; but every now and then one will meet cases of hemorrhage which for some reason resist ordinary treatment on account of their position, which cannot be reached; in these cases gelatin should be tried. Jaboulay advocates the prophylactic injections of gelatin before any operation in which the surgeon may fear that hemorrhage might take place or in those patients in which a very slight hemorrhage might be disastrous. I can find no cases in the literature in which one has used such injections previous to operations on hæmophylic patients. Bass gives the following conclusions:

1. The gelatin salt solution (gelatin serum) increases the coagulability of the normal as well as the pathologically changed blood.

2. The increase in the coagulability shows in the direct contact with the blood (local application) as well as in the subcutaneous injection.

3. The gelatin presents not only a harmless, but also a coagulation-aiding agent, which, owing to its nutritive properties, furthers the organization of the thrombus and produces, with the proper particular aseptic precautions, no local or general symptoms of irritation.

4. From this follows the applicability of the gelatin serum to the treatment of external and internal hemorrhages of individuals with healthy blood, as well as of hæmophylic and cholæmic individuals in particular. An experiment in brain hemorrhage has not yet been made.

5. The value of the prophylactic pre-operative injections of gelatin requires further investigation.

6. The concentration of the gelatin should be 1 to 2 per cent. for subcutaneous ; 5 to 10 per cent. for local application. The temperature should be from 37° to 38° C.

7. Only absolute sterile gelatin may be used.

8. As the chief counterindication to be considered, the presence of heart or kidney affections. Neither Bass nor his authorities quoted go into the reasons for the contraindication of gelatin in heart and kidney diseases.

There are some instances where the surgeon has attempted to operate without the use of the hæmostatic forceps by previously using gelatin injections and local applications ; but in all of these cases, if the operation was at all extensive, there has been hemorrhage ; in a few quite serious. I do not believe that such a procedure is justified, as in every surgical operation the ordinary means of checking hemorrhage (the hæmostatic forceps and ligature) should never be neglected. But there are some operations (as in hæmophylia and in jaundice, and now and then in patients with marked anæmia) in which there is a constant oozing from the cut tissues which cannot be checked by ordinary means. It is in such cases that gelatin should be used, and judging from the experience already gained it will be of value. I am surprised to see how seldom it has been tried in severe hemorrhages from the intestines associated with typhoid fever or obstructive jaundice, many of which have been fatal ; also in hemorrhages from the stomach especially associated with ulcer. There are a sufficient number of cases in the literature to make it imperative for both surgeons and physicians to use gelatin in these cases.

The test for the coagulability of the blood is not a difficult one to make, and this test should be an index for the use of gelatin in pathological conditions. Now and then, of course, we will wish to increase

the coagulability of the normal blood ; but, on the whole, except perhaps for aneurism and extensive hemorrhages from ulcerated surfaces, the more frequent and important use of gelatin will be in those cases in which the coagulability of the blood is greatly reduced and yet in which operative procedures are indicated.

**The Use of Gelatin Injections in Aneurism.** The results here have not been as satisfactory as in other conditions. An exhaustive review of the literature was made about a year ago by Sorgo.<sup>1</sup> Fletcher<sup>2</sup> reports interesting results from experience with gelatin injections in Dr. Osler's wards.

## SALT-WATER INFUSION.

**The Method and Therapeutic Value of Salt-water Infusion.** Within the last few months there have been three rather extensive and very comprehensive articles on this important subject. We have first a collective review of the entire literature by Leopold Laufer,<sup>3</sup> of Vienna ; a second one by Georgii,<sup>4</sup> of Rottenburg, and a third by Hermann Lenhartz.<sup>5</sup> Laufer's collective review is at least twenty-five pages. In addition to the history and complete reference to the literature, he considers the subject from every point of view, not only from the clinical side, but from the theoretical and experimental. Georgii's article, of almost the same length, is directed chiefly to the usefulness of infusion in general medical practice, and is a plea for the more extended use of infusion by the general practitioner in various conditions. Lenhartz directs his attention to the therapeutic value of the salt-water infusion in acute diseases.

**Methods of Infusion.** Practically the older method of blood transfusion and the later method of infusion of defibrinated blood has given way to the infusion of some form of saline solution. This change is due to the difficulties and dangers of blood transfusion or defibrinated blood infusion as compared with the simplicity and practically harmless method of saline infusion, the latter, supported by experimental and clinical observation, demonstrating that the salt solution gives as good and perhaps better results than the older methods. An infusion may be given subcutaneously, intravenously, in the artery, per rectum, or intraperitoneally.

All authorities agree, with few exceptions, that the subcutaneous method of infusion gives equally good results, with practically no

<sup>1</sup> Centralbl. f. die Grenzgebiete der Med. u. Chir., 1899, p. 10.

<sup>2</sup> Johns Hopkins Hospital Bulletin, May, 1899, vol. x., p. 29.

<sup>3</sup> Centralblatt f. die Grenzgebiete der Med. u. Chir., 1900, Bd. iii., Nos. 11, 12, and 13.

<sup>4</sup> Münch. med. Wochenschr., July 11, 1899, 46 Jahr.

<sup>5</sup> Deut. Arch. f. klin. Med., 1899, Bd. lxiv., p. 189.

serious consequences. The intravenous infusion is a more difficult operation, requires more instruments and a better technique, and is not devoid of danger. To the general practitioner at the bedside of the patient (not in the hospital), with no assistance, intravenous transfusion is a somewhat formidable operation. Even in a hospital, with all the necessary paraphernalia and assistance, it takes more time than the subcutaneous method. So that one would choose the intravenous method only in those few cases in which experience has demonstrated that it is distinctly indicated in addition to the subcutaneous infusion. The chief danger of introducing blood into the vein is from air emboli or a clotting of the blood, followed by an embolus. The infusion of defibrinated blood or saline solution into a peripheral artery is not discussed by these three authorities. It is, however, an established method, but seldom used at the present time. The only advantage that it has over the intravenous is that the danger of air or other emboli is excluded. It is, however, a more delicate operation to infuse in the artery, and now and then an embolus has plugged the artery, and gangrene of the hand or foot has followed; so that, although it has not the same dangers to life, the possibility of gangrene must be borne in mind. If one is using defibrinated blood it is probably safer to infuse it through an artery. Prof. Halsted<sup>1</sup> demonstrated this in his experience in New York, many years ago, in the treatment of patients asphyxiated with illuminating-gas. Halsted recommends centripetal arterial infusion.

**The Method of Intravenous Transfusion.** One should have the necessary instruments conveniently arranged; the arm of the patient should be carefully cleansed, and any superficial vein near the elbow may be chosen. It should be exposed with an incision made after Schleich's infiltration cocaine anæsthesia. The vein should be isolated; two ligatures tied at about a centimetre distance apart; the vein opened in a longitudinal direction; the canula, which is attached to the rubber tubing and filled with salt solution, should be introduced and the proximal ligature loosened; the canula passed beyond the ligature, which is again tightened, and the solution allowed to pass slowly into the vein. The solution should be kept at about a temperature of 100° F.; the infusion should be slowly made, taking at least one-half to three-quarters of an hour to infuse 500 to 1000 c.c. The rapidity of the flow is regulated by the height of the vessel which holds the solution. In some cases it may be justifiable to transfuse a little more rapidly. In my own experience and that of others in Baltimore who have used this method I have never seen a serious result, although a rise of tempera-

<sup>1</sup> *Annals of Anatomy and Surgery*, January, 1884.

ture and chill usually follow the infusion. It would appear from the experience of many writers that the intravenous infusion should be used in certain cases, namely, in those patients in whom we wish to do a phlebotomy with bleeding. Here we may utilize the same vein that we divide, or, better, the infusion should be taking place through one vein of the opposite arm while we allow the patient to bleed a sufficient quantity at intervals from the other arm. In cases of very acute infection and poisoning, in which it is considered best to allow some of the poisoned blood to flow out of the vessels and at the same time to replace the fluid by infusion of salt, here, at least during the bleeding, the intravenous transfusion is the better method. In some cases of extreme shock from hemorrhage, or collapse from cerebral injuries, or extreme conditions of collapse from any cause in which the vasomotor tone is practically *nil*, a rapid intravenous transfusion will restore the vasomotor tone much more quickly than any other method, and in many instances will be the only factor which preserves life. With these exceptions there is no better method than the subcutaneous infusion.

**Intraperitoneal Infusion.** There is no indication for the infusion of salt solution into the peritoneal cavity unless there has been a laparotomy. In such instances the flushing of the peritoneal cavity with salt solution, and when the abdominal wound is closed, leaving the peritoneal cavity filled with a certain amount of salt solution, is an important therapeutic agent. The work of John G. Clark<sup>1</sup> and others is very suggestive in this direction. In the normal peritoneal cavity, with no evidence of local or general peritonitis, flushing of the peritoneal cavity at the end of the operation and the leaving of some fluid in it is an important treatment in post-operative shock. Clark used it as a routine procedure after every case of laparotomy for the following reasons:

1. To supply fluid and thus to alleviate thirst for the first few days, during which time the patient is unable to take much water by the mouth.

2. As a preventive to possible post-operative infection. The experience of Clark and others and some experimental work seem to show that this salt solution in the peritoneal cavity, with the elevation of the foot of the bed, aids in taking care of any possible infection by increasing the lymphatic absorption. In different forms of local, and especially general peritonitis, the absolute value of flushing of the peritoneal cavity and leaving the peritoneal cavity full of salt solution after the operation is an unsettled problem. On the whole, experience teaches if the infection is a local one it is better to leave the general peritoneal

<sup>1</sup> Johns Hopkins Hospital Reports, 1899, vol. vii., and PROGRESSIVE MEDICINE, June, 1900.

cavity alone. Flushing of the local infected area can hardly be done without great danger of infecting the general peritoneal cavity. However, in the event that the general peritoneal cavity is infected either previous to operation or during operation it is pretty well established that irrigating done gently and not too long is a good method to wash away the infected material; and, on the whole, from the work of Clark and others, it would seem the better plan when the wound was closed or drained to leave in the peritoneal cavity some salt solution. This subject, however, is one in which there is room for a more extended and careful clinical observation and more thorough experimental work.

**Infusion per Rectum.** This has only a limited field. One should never depend upon rectal absorption in the treatment of shock or in any critical condition. In such cases the subcutaneous or intravenous method should always be used. However, there are certain cases in which the salt enemata can be used in addition to the subcutaneous infusion, and there are some cases in which the salt enemata are sufficient. It is the rule now in Prof. Kelly's clinic at the end of every operation to give a salt enema per rectum, and they have given up Clark's method of leaving salt solution in the peritoneal cavity after every laparotomy. This salt solution is placed in the lower bowel after every operation for the treatment of slight post-operative shock or for prophylactic treatment of post-operative shock and to prevent post-operative thirst. On the whole, I would prefer a subcutaneous infusion in the majority of cases to this routine post-operative rectal infusion. It is important in many cases to use rectal infusion in conjunction with and in addition to subcutaneous infusion, and in those cases in which the rectum is not irritated by it and in which the enemata are not expelled. For example, in traumatic or post-operative shock, in addition to the subcutaneous infusion, one should always give hot rectal enemata. The rectal infusion can always be of a higher temperature than the subcutaneous or intravenous infusion from 105° to 108° F. In addition to the salt one may add coffee, which is an excellent stimulant. In infections and in any condition, post-operative or not, when one wishes to give infusions at intervals of two or four hours, the subcutaneous one becomes painful; so that we give the subcutaneous infusion every six, eight, or twelve hours, and in the interval 200 to 300 c.c. of salt solution is introduced with a medium-sized catheter high up in the rectum. If given carefully with a catheter (instead of the usual rectal tube), if given high, and if not combined with whiskey or other irritant medication, the rectum will bear salt infusions every two hours for a number of days and frequently some weeks—an interval of time sufficiently long for the treatment of almost every condition in which it is indicated. Now and then one will find that an enema of 300 or 400 c.c.



of salt solution and a half to one ounce of whiskey given at night will produce sleep in very weak individuals in whom we wish to save the stomach for nutrition only. I have observed from a very large experience in Prof. Halsted's clinic that the greatest care must be exercised when repeated rectal enemata are given, either of salt solution or peptonized milk. The most important fact is that whiskey is very irritating. It may be given once in twenty-four hours, but seldom should be given more frequently if one wishes to use the rectum for a number of days.

**The Subcutaneous Method.** All authorities agree, with few exceptions, that this is the method of choice. The procedure is a very simple one. One should have a fountain syringe or any form of vessel to which is attached a rubber tube. To the end of the rubber tube is attached an ordinary aspirating needle of medium size. The whole should be sterilized by boiling, which can be done in a moment. The vessel is filled with salt solution about the temperature of 100° F. There seems to be no danger if the temperature is 102° or 103° F. The skin through which the puncture has been made should be carefully cleaned; alcohol followed by bichloride, 1:1000, is, as a rule, sufficient. If, however, the case is one of infection—I mean by this an infected wound in another part of the body—or when one is in unusually uncleanly surroundings, the cleansing of the skin should be more careful and of longer duration. The introduction of the needle is seldom painful. Perhaps in nervous patients one might infiltrate with cocaine a small wheal, through which the infusion needle can be introduced. The needle should pierce the skin and the subcutaneous tissue, and, if possible, the fluid should be infused inter-muscularly. The place of selection is a pectoral region in the male or female. The needle should pass between the fascia of the breast and the pectoral fascia on the axillary side of the breast. In this area there are a great many vessels, the circulation is good, the tissue is loose, and one can infuse a litre of salt rapidly without pain and with practically no danger of bad after-effects. The fluid infiltrates between the breast and the pectoral muscle and then into the loose tissue in the axillary fossa. Unless there is a distinct contraindication (and there seldom is such) this position should be selected; even in the youngest children it is available. A second infusion can be made in the same place in four to six hours without harm. It is better, however, at the second infusion to use the opposite side. The buttocks, the outer lateral surface of the thigh, the lumbar region, the abdominal wall, and the muscle over the scapula have all been used. There is a distinct objection to the buttocks, especially for the infusion of any amount, as the fat in this region is not vascular, the circulation does not compare with that of the axilla,

and pressure is frequently followed by gangrene. The same is true in the thigh infusion beneath the tense fascia lata. In a number of cases it has been followed by a large localized area of gangrene of the skin, in many instances including the fascia and extending down to the muscle. After infusion in the region of the breast there have been a few cases of infection.<sup>1</sup> Most of these, however, were associated with bad technique. I have observed but one infection in a great many instances of infusions; in this case a chronic mastitis developed. The patient returned six months later with a beginning abscess. In this instance, however, the assistant plunged the needle directly into the breast tissue, and there was without doubt distinct necrosis from distention. As Georgii emphatically says, not only the surgeon but every practitioner should have a transfusion apparatus in his armamentarium, and should familiarize himself with the simplicity of the method. The fountain syringe with a needle can be boiled in a few minutes, or for emergency cases it can be kept sterilized wrapped in two towels. It takes but a few minutes to sterilize the skin; boiled water, to which the salt can be rapidly added, is generally of easy access, so that a subcutaneous infusion should be but a matter of five or ten minutes. Benkiser recommends that all druggists should have prepared for immediate use the sterilized infusion apparatus and a sterilized salt solution. This is a very good suggestion and will be a great help to the general practitioner. As far as the surgeon, the gynecologist, and the obstetrician are concerned, I feel that it is almost criminal for any of them to be ever without an infusion apparatus.

In addition to the careful technique, the subcutaneous transfusion should be done, as a rule, slowly; say, about thirty minutes for 500 c.c., and during this time gentle massage should be made of the infusion tumor to aid absorption.

**The Choice of the Solution for Infusion.** On this subject a great deal has been written, and there has been much conscientious experimental work. On the whole, most authorities agree that the chief value of the infusion is its quantitative and not its qualitative supply to the blood; so that we wish a solution which, when introduced into the circulation, will supply a fluid which is not only not irritating to the tissues, but which has no bad effects upon the cellular or fluid elements of the blood. Dawson<sup>2</sup> has studied this subject in the laboratory of physiology in the Johns Hopkins University, and in his article entitled "Effects of Venous Hemorrhage and Intravenous Infusion in Dogs" he has studied the following solutions:

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1899.

<sup>2</sup> American Journal of Physiology, May 1, 1900, vol. iv.

|                                |       |       |                            |       |        |                            |
|--------------------------------|-------|-------|----------------------------|-------|--------|----------------------------|
| 1. Normal saline . . . . .     | No. 1 | 0.8   | p. c. NaCl.                | No. 2 | 1.0    | p. c. NaCl.                |
| 2. Ringer's solution . . . . . | No. 1 | 0.8   | p. c. NaCl.                | No. 2 | 0.8    | p. c. NaCl.                |
|                                |       | 0.026 | p. c. CaCl <sub>2</sub> .  |       | 0.01   | p. c. CaCl <sub>2</sub> .  |
|                                |       | 0.03  | p. c. KCl.                 |       | 0.01   | p. c. NaHCO <sub>3</sub> . |
|                                |       |       |                            |       | 0.0075 | KCl.                       |
| 3. Milk . . . . .              |       | 0.8   | p. c. NaCl 10 parts.       |       |        |                            |
|                                |       |       | Milk, 1 part.              |       |        |                            |
| 4. Alkaline solution . . . . . |       | 0.8   | p. c. NaCl.                |       |        |                            |
|                                |       | 0.5   | p. c. NaHCO <sub>3</sub> . |       |        |                            |

He states the following conclusions :

1. From observations on the pulse and respiration there is no evidence that variations (within the limits described) in the composition of the fluid infused have any influence on the immediate recovery of the animal.

2. Examinations of the blood afford no evidence that such variations have any influence on the character and rapidity of the regeneration of the blood.

3. Ringer's solution containing as much as 0.026 per cent. of CaCl<sub>2</sub> is dangerous (Ringer's solution No. 1).

From Dawson's observations, therefore (and others), Ringer's solution No. 1 should not be used in transfusion. In one of Dawson's cases he attributes the death of the dog to this solution. Dawson's experiments show that there is always a post-hemorrhagic leucocytosis, which has already been discussed on page 100. From this and other experimental work, as well as clinical observations, normal salt solution seems to be on the whole the best fluid for infusion.

**Conditions in which Infusion Should be Practised.** The therapeutic value of a saline infusion is to replace fluid which has been lost by hemorrhage or to replace the fluid in the body which has been lost by excessive excretions, especially in the different forms of diarrhœa. In all conditions in which there are poisons or toxins circulating in the blood the saline infusions are unquestionably valuable in diluting such poisons, and in addition increase the power of at least the kidneys, and perhaps the intestine and skin, in the excretion of the poison. Experimental and clinical evidence distinctly show that saline infusion increases the vasomotor tone and stimulates the excretion of fluid from the kidney—not only the quantity of the fluid, but its organic and inorganic constituents. If the patient is bleeding, and one is not able to check the point of hemorrhage, there is no experimental or clinical evidence against using saline infusion, as it does not increase the hemorrhage; although there seems to be a general impression that in collapse from concussion and compression of the brain infusion is contraindicated. This, however, is not so. In traumatic or post-operative shock, whether associated or not with loss of blood, infusion is always indicated, and in

every case of injury, whether there has been great blood loss or not, subcutaneous infusion should be practised at once. The subcutaneous infusion combined with rectal enemata should be continued in all cases of shock, especially in those associated with great loss of blood, until the symptoms of reaction set in; sometimes for a period of two or three days.

On the operating-table the subcutaneous infusion should be made the moment the symptoms of shock appear; one should not wait until the patient is collapsed. It is an excellent plan after all operations in weak patients, whether there are symptoms of shock or not, to give at least one prophylactic subcutaneous infusion of from 300 to 500 c.c. of salt solution, and especially in those cases of laparotomy in which, on account of the condition of the stomach, it will be impossible to give sufficient fluid by the mouth, and in which the rectum does not retain enemata well, the subcutaneous infusion should be continued at intervals of six to eight hours for three or four days. As a routine it seems pretty thoroughly established that the function of the kidney is much better performed and the danger of uræmia very much less. From the large experience of many operators it would appear that it is an excellent routine plan in all cases of nephritis or infections of the genito-urinary tract to give previous to, during, and for some days after operation subcutaneous infusions of salt combined, if possible, with rectal enemata, in the hope of preventing uræmia, which in these cases has in the past been so frequently the cause of death. In all grave surgical infections, especially with the streptococcus, routine subcutaneous infusion three to four times in twenty-four hours is a very important aid in carrying the patient through this critical period. It should be practised in all cases of general peritonitis and after operation for a number of days. It has proved of distinctive value in cases of pneumonia, especially in the septic post-operative bronchopneumonia. The use of infusion in medical practice can hardly be discussed here, but it has been found of the utmost value in all cases in which excessive fluid has been lost through the intestines; it has proved valuable in persistent vomiting; and it has unquestionably saved cases of diabetic coma. There have been numbers of clinical observations where its therapeutic value cannot be questioned in all forms of poisoning, even in strychnine poison. In obstetrics, in addition to its practically life-saving service in sudden hemorrhages, it is the most important adjunct to phlebotomy with bleeding in peripheral eclampsia.

Every surgeon and practitioner should familiarize himself at once with the technique of at least subcutaneous transfusion, and should always have not only the apparatus but the solutions ready for immediate use.

## ANÆSTHESIA.

**The Selection of the Anæsthetic in Surgery.** I have gone over the literature from 1898 to 1900, a period of about two years, in which I found many articles, including a *résumé* of much of the past literature. We still find the greatest difference of opinion in regard to the selection of the anæsthetic, even in surgeons with great experience and in large clinics. Wyeth,<sup>1</sup> in his discussion on anæsthesia before the New York Medical Association, states that in his first ten years of service at Mount Sinai Hospital and the New York Polyclinic as well as in private practice he employed ether exclusively. From time to time he observed not only a very great irritation which the vapor of ether caused to the respiratory tract, but that in a certain proportion of cases, especially in alcoholic subjects, it was extremely difficult to procure profound narcosis without inducing a threatening condition of asphyxia. Such annoyance he has observed to be entirely absent in chloroform narcosis, and the comfort when chloroform was used, both to the patient and operator, encouraged him to its more frequent use. At present Dr. Wyeth employs chloroform in about 75 per cent. of his operations, either wholly or at some stage of the narcosis. Previous to its administration he always gives  $\frac{1}{4}$  grain of morphine and  $\frac{1}{160}$  grain of atropine subcutaneously. He thinks that the combination of these alkaloids stimulates the heart and allays to a considerable extent the anxiety of the patient. Their employment is based on what he believes to be a fact, that chloroform is dangerous chiefly to the heart, especially in the early stages of administration. Chloroform, however, he thinks should be administered with the greatest care and only by one thoroughly trained in its use.

Wyeth states that in children he believes that ether is the safer general anæsthetic, although in the early days of his career he had been taught that chloroform was safer. Here we have the opinion of a surgeon of large experience in favor of chloroform as a general anæsthetic in the majority of cases, except in children. However, Dr. Wyeth gives only his impressions over a number of years of experience, and frequently our impressions are wrong. One can only judge in regard to ether and chloroform by a great number of cases carefully studied and carefully tabulated.

In contradiction of Dr. Wyeth we have the publication of Dr. Blake,<sup>2</sup> of Boston, under the title "Administration of Ether at the Boston City Hospital." Dr. Blake writes: "There is little doubt that proportion-

<sup>1</sup> Journal of the American Medical Association, March 24, 1900, vol. xxxiv.

<sup>2</sup> Boston Medical and Surgical Journal, September 28, 1899, vol. cxli.

ately more ether is used in Boston than in any other city in the world. A keen interest in the administration of ether always exists in this vicinity, and has, for various reasons, increased rather than declined during the last two years. This is probably true the world over, and is in part due to the work of Schleich in both local and general anæsthesia, and the recent statistics of Gurlt in Germany and of the St. Bartholomew's Hospital in London." Blake then follows with a detailed description of the routine method of etherization in the Boston City Hospital. He feels that three things have combined to increase the attention paid to the administration of ether as well as the personal interest taken: (1) The establishment of the Burrell ether prize; (2) the visit of Dr. Bennett, a professional anæsthetist from New York, and (3) the introduction of the ether chart. Dr. Bennett demonstrated in Boston the gas-ether apparatus, and production of the anæsthesia was so easy, so rapid, and, apparently, so pleasant that it could not fail to excite the admiration of all. Unquestionably it has a good effect upon both the undergraduate students and the hospital internes to witness anæsthesia properly administered by a skilled anæsthetist; it undoubtedly stimulates them to more careful observation of their own cases and a greater ambition to improve their methods. Dr. Blake refers to the chart used at the Johns Hopkins Hospital, which they have slightly modified. This chart was introduced at the Johns Hopkins Hospital by Dr. Cushing, and I am glad to see that it has had the same good effect in Boston as with us in Baltimore. It unquestionably stimulates the anæsthetist to a more careful observation of his patient at almost every moment during the operation. To have on the chart, which can be referred to at any moment, a record of the pulse from the time ether was administered is a great help to the operator. On this chart the pulse is recorded every five minutes. Unquestionably in Boston ether is the anæsthetic of choice, and so far the use of nitrous oxide preliminary to ether has been used only in a few cases. The use of oxygen is also restricted to a few cases in which it is especially indicated. Blake agrees with Wyeth in the use of atropine (grain  $\frac{1}{100}$ ) previous to the beginning of the anæsthesia. He thinks it has been decidedly beneficial in diminishing vomiting and diminishing the amount of secretion in the mouth and air passages. He states, however, that it is a direct stimulation to respiration, while Wyeth uses it to stimulate the heart. Blake concludes with the statement that he is satisfied that ether is given, on an average, better in and about Boston than in any other place in the world, with the possible exception of London, and that the methods of anæsthetization are distinctly better in the City Hospital in the last few years. He thinks the complications following ether are less frequent, as he has noted only one case of pneumonia after ether. Such statements,

however, should be followed by a careful statistical study of all the cases. Unquestionably it would be a very important contribution from a city like Boston, with so many great surgical clinics in which ether alone has been the chief anæsthetic, to have a careful statistical study.

**The Later Effects of the General Anæsthetic.** Hobart A. Hare<sup>1</sup> has called attention to this in a discussion on anæsthesia in the Section on General Surgery of the College of Physicians of Philadelphia. He writes: "Recovery from the operation may be satisfactory; the physician who has the patient sent back to him sees nervous manifestations, which if he is a careful student of his case will impress him with the fact that while there has been an operative recovery, the patient for weeks and months after the operation has distinct evidence of nervous shock." The ultimate health of the patient after general narcosis has not been carefully studied. Dr. Hare unquestionably, however, is right, that in a certain number of cases there is a distinct post-operative condition of depression, which may last a long time and which requires especial care and careful treatment, and should never be lost sight of after the patient has left the hospital. I cannot, however, agree with Dr. Hare that the surgeon by seeing a large number of patients brought under an anæsthetic day after day unconsciously becomes somewhat hardened to the condition. I believe that the greater the experience of the surgeon in anæsthesia the more he fears the anæsthetic and the more careful he becomes in the methods of its selection and administration.

The immediate post-operative dangers and complications of the general anæsthetic are only sufficiently numerous to impress forcibly the surgeons of larger experience, and I believe that in large clinics all over the world that attempts for improvement in general anæsthesia are being made. Personally, I have made the most careful study of the immediate and ultimate effects of the general anæsthesia on 459 operations for inguinal hernia.<sup>2</sup> In view of the facts obtained I found that I was able to state to the ordinary patients suffering with a non-strangulated hernia, that the probabilities of death were less than one-half of 1 per cent.; of pneumonia, 1.2 per cent.; of phlebitis of the leg, 0.7 per cent. The causes of death in non-strangulated hernia in 395 cases were: one boy of six years died on the seventh day with diphtheritic colitis. It was a question in this case whether it was a coincident or whether the colitis was due to absorption following the irrigation of the wound with 1:1000 of bichloride. Acute dysentery following ether after an operation for hernia had been observed but twice in a group of 443 cases, one of which died. From other observations we now and

<sup>1</sup> *Annals of Surgery*, 1898, vol. xxviii., p. 274.

<sup>2</sup> *Johns Hopkins Hospital Reports*, 1899, vol. vii.

then see marked intestinal disturbances following ether. In a second case, an apparently perfectly healthy young woman, aged thirty-six years, died suddenly on the tenth day from an embolus to the left pulmonary artery, originating from thrombosis of the left internal iliac vein. In the study of 10,000 cases in Halsted's clinic this has been the cause of death in one case. In a similar observation in Dr. Kelly's service the proportion was about the same. This possibility of death following general anæsthesia must always be borne in mind. In the group of forty-eight cases of strangulated hernia in which the contents of the sac were in good condition there were four deaths, or 8 per cent. In one case the patient died suddenly on the tenth day, and the autopsy showed arteritis of the coronary arteries. Sudden death in various heart lesions is so common that it is strange that they are not more frequently observed coincident with various operations. In a second case a hydronephrosis of long duration became infected after an operation for a strangulated femoral hernia, due perhaps to the lowered resistance and necessary catheterization. On the ninth day the right hydronephrotic kidney was opened under ether; the patient died in a few hours with anuria; the opposite kidney at the autopsy was apparently healthy. I have observed that anuria was the cause of death following ether in five other instances—one from a strangulated umbilical hernia coming under observation after the publication of my paper. In the third case the cause of death can be attributed directly to the anæsthetic; the patient died ten minutes after the beginning of the ether, and at the autopsy a gumma of the cerebellum was found. I believe in this case the operation on the strangulated hernia with the local anæsthesia would have given a different result. In the fourth case—a strangulated umbilical hernia—the patient died on the third day from pneumonia. In this case, also, I believe the result would have been different from local anæsthesia. In non-strangulated hernia (395 cases) pneumonia followed the ether in five cases, or 1.2 per cent. Of these five cases, which apparently recovered and left the hospital, two died within a year of tuberculosis of the lungs. This observation must be borne in mind in the estimation of the mortality of pneumonia following the anæsthesia. In strangulated hernia, forty-eight cases, pneumonia was noted in one case, and was the cause of death. However, in strangulated hernia in which the contents of the sac was gangrenous intestine or in which a general peritonitis was present (sixteen cases) pneumonia was found at the autopsy in 25 per cent. of the cases; in all but one it was associated with general peritonitis; in this one case pneumonia was the cause of death. Chloroform administered for thirty-five minutes was the anæsthetic. The resected and sutured intestine was successful; there was no evidence of peritoneal infection.



So far in our experience in local anæsthesia we have observed no deaths or complications which could be attributed to the anæsthetic. There have been no cases of pneumonia and not a single case of phlebitis of the leg. We have been unable to observe any bad effects upon the kidneys. This comparison is a very important one, because the patients subjected to the general anæsthesia were, as a rule, the selected ones, while those subjected to local anæsthesia were in the majority of instances individuals suffering from some condition contraindicating the use of a general anæsthetic.

### LUMBAR PUNCTURE.

Quinke's method of *lumbar puncture* is quoted by all following authorities. Now that it has become such a common procedure not only for diagnosis, but even for treatment, the method should be understood by every practitioner. It is an operation which the physician as well as the surgeon should be able to perform. I have been unable to find a description of it in any ordinary text-book in English. Quinke writes: "The needle should penetrate between the vertebra in a median line, and as we know the spinal cord ends in children at the third and in adults at the second lumbar vertebra, the needle should then pierce the canal in a position below the cord, to avoid the injury of it. Therefore, one selects in adults the second or third intervertebral space; in children the third or fourth. The puncture should be made in a median line." In a child Quinke states the puncture of the skin should be in a median line, while in an adult one thrusts the needle into the skin a few millimetres to the right of the median line, but directs it slightly medially and upward, so that the dura of the canal, however, is pierced in a median line. Previous to the puncture, of course, the skin should be properly sterilized, as well as the instruments used and the hands of the operator. This is not only important, to prevent infection of the tissues and the spinal fluid, but when one wishes to make a bacteriological examination of the fluid from the spinal canal one's technique should be additionally careful. Quinke's article deals entirely with the diagnostic value of lumbar puncture, the methods of measuring the degree of pressure, and the chemical and bacteriological study of the fluid, which need not be considered here. Quinke demonstrated the possibility and the value of lumbar puncture for diagnostic purposes and opened the field for its use for therapeutic purposes.

**Lumbar Puncture for Diagnostic Purposes.** In recent years this has become additionally important from the work on cerebro-spinal meningitis. Councilman, Mallory, and Wright, of Boston,<sup>1</sup> write that

<sup>1</sup> Epidemic Cerebro-spinal Meningitis and its Relations to Other Forms of Meningitis. A Report of the State Board of Health of Massachusetts, Boston, 1898, p. 79.

they have performed lumbar puncture for diagnostic purposes in fifty-three cases ; several punctures were made. In each case fluid was obtained for bacteriological study. They describe the technique as follows : First, the usual sterilization of the patient's skin, hands of operator, and instruments. The patient should lie on his right side, with the knees drawn up, and have the uppermost shoulder so depressed as to present the spinal column to the operator. In addition to this the suggestion of Quinke should be followed. The back should be arched, especially in the lumbar region. This throws the spinous processes of the lumbar vertebræ apart and increases the intervertebral space for the injection of the needle. The puncture is generally made between the third and fourth lumbar vertebra, sometimes between the second and third. The thumb of the left hand is pressed between the spinous processes, and the point of the needle is entered about 1 cm. to the right, of the median line (Quinke states that in children it should be entered in the middle line) and on a level with the thumb-nail. Care must be exercised to prevent the needle from passing to the left of the median line and striking the bone. At the depth of 3 to 4 cm. in children and 7 to 8 cm. in adults the needle enters the subarachnoid space, and the fluid flows usually by drops. If the point of the needle meets with the bony obstruction it is advisable to withdraw the needle somewhat and to thrust again, directing the point of the needle toward the median line rather than make lateral movements, with the danger of breaking the needle or causing hemorrhage. Fluid is allowed to drop into absolutely clean test-tubes, which previously have been sterilized. These writers, with this large experience, state that they have never had ill effects from spinal puncture. In some cases the withdrawal of fluid has been followed by positive benefit to the patient. These authorities recommend the ordinary antitoxin needle, 4 cm. in length and about 1 mm. in width, for infants and children ; longer needles for adults and children over ten years of age. Quinke, however, recommends a canula with a trocar, believing that the danger of injury to the nerves of the cauda equina is less. This instrument, with its blunter point, pushes the nerves aside and does not pierce them. He states that in the experience of other observers who use the ordinary sharp-pointed aspirating needles some bad results have followed. This, however, has not been the experience of Councilman, Mallory, and Wright, nor of Osler.

Dr. Fletcher, resident physician of the Johns Hopkins Hospital, informs me that they have performed in Dr. Osler's wards lumbar puncture for diagnostic purposes in about seventy-five instances. They used an ordinary aspirating needle, which is introduced in the manner already described. If the fluid does not flow at once they have a small wire

stilette, which is passed through the lumen of the needle. This is frequently necessary, as the end may become plugged up with pieces of fibrin, by suction, or a piece of membrane or nerve. He also informed me that they have had no disagreeable results during or after the lumbar puncture. In a recent case seen with him and Dr. Mitchell, the resident surgeon, the lumbar puncture was of important diagnostic service. The child had the symptoms of cerebro-spinal meningitis of short duration and a history of a longer duration of a discharge from the left ear. The demonstration of a pure culture of the pneumococcus in the cerebro-spinal fluid indicated that the infection was, without much doubt, from the ear, and not a case of epidemic cerebro-spinal meningitis, which is associated with its own specific form of micrococcus.

**Lumbar Puncture for Therapeutic Purposes.** Frank Hahn,<sup>1</sup> of Vienna, in a collective review of the literature on the application of cocaine to the spinal marrow (Bier's method), informs us that the first experiments in the direction of therapy by lumbar puncture were made in 1898 by Siccard.<sup>2</sup> He injected animals in the subarachnoid space with various substances, and demonstrated that the subarachnoid cavity could without difficulty receive large doses of fluids, which were quickly absorbed, and found that these substances could act therapeutically. He demonstrated that not only the injection but the absorption of the drug was better in the lumbar region, and that this position permits the injection of greater quantities of fluid (from 200 to 300 grammes). The injected fluids penetrate quickly into the subarachnoid spaces and are rapidly diffused there. Also the important fact was demonstrated that the effect of these introduced fluids on the centres situated higher than the lumbar was much slighter; only the very oily and gaseous substances ascend and influence the higher centres. The reabsorption of the water solutions so injected by the central nervous system takes place in two ways: (1) Very rapidly through osmosis and (2) more slowly through leucocytic diapedesis. It is also important that concerning the dose of the injected drug much smaller quantities are required in the subarachnoid injection to produce the same desired therapeutic effect than in subcutaneous and intravenous injections of the same drug. This fact, as well as the great rapidity with which the action takes effect on the nervous centres, proves the great therapeutic importance of this method. Jaboulay<sup>3</sup> injected tetanus serum in a case of paralysis agitans in a patient

<sup>1</sup> Centralbl. f. die Grenzgebiete der Medizin und Chirurgie, May 8, 1900, Bd. iii., No. 9, p. 337.

<sup>2</sup> Essais d'injections microbiennes, toxiques et therapeutiques par voie cephalo-rachidienne. Compt.-rend. des seances de la Société de Biologie, April 30, 1898.

<sup>3</sup> Injections de liquides medicamenteux dans les meninges. Lyon Médical, 1898, Bd. lxxxviii., No. 20.

suffering from general contractures. There was no result therapeutically, but there were no injurious after-effects. Jakob<sup>1</sup> injected iodine solutions and chloral hydrate, demonstrating that the injection of great quantities of these fluids in a healthy individual does no harm, and that the injected fluid was actually reabsorbed by the nervous central organs and remained there for some time. Other investigators have demonstrated that with the method of Quincke's lumbar punctures practically any therapeutic agent may be introduced into the system in this way.

### INFECTIONS.

**Emphysematous Cellulitis (Gas Bacillus Infection).** In PROGRESSIVE MEDICINE for December, 1899, I devoted seventeen pages to this very important subject, chiefly because it is an infection not well understood by the general profession in this country and because an early diagnosis followed by operative treatment yields most brilliant results. The cases reported in that article clearly demonstrate this. Professor William H. Welch, in the Shattuck Lecture,<sup>2</sup> considers most exhaustively the morbid conditions caused by the bacillus *aërogenes capsulatus* (the gas bacillus),<sup>3</sup> with a most extensive *résumé* of the literature. I consider myself most fortunate in being able to review this article, because it has made clear a number of important points which seem to have been misunderstood by the great majority of writers. It is especially interesting and instructive to have this contribution on the gas bacillus from Dr. Welch, who was first to recognize it, and who, with Dr. Nuttall and Dr. Flexner, had already given us two excellent publications.

THE DIFFERENTIAL DIAGNOSIS BETWEEN EMPHYSEMATOUS CELLULITIS (OR EMPHYSEMATOUS GANGRENE) AND MALIGNANT ŒDEMA. With hardly an exception most text-books and most clinicians do not differentiate malignant œdema from emphysematous gangrene, and many cases reported as malignant œdema are unquestionably due to the gas bacillus isolated by Dr. Welch. He writes as follows: "A critical examination of the records of alleged malignant œdema in human beings shows that in very few was the organism concerned satisfactorily identified as the genuine malignant œdema bacillus. Very often has it been simply assumed without more than a microscopical examination that the bacilli found in spreading œdematous conditions, with or without gas, have been those of malignant œdema; and even where cultures and

<sup>1</sup> Berl. klin. Wochenschr., 1898, Bd. xxxv., Nos. 21 and 22.

<sup>2</sup> Delivered before the Massachusetts Medical Society, June 12, 1900.

<sup>3</sup> Boston Medical and Surgical Journal, July 26, 1900; Johns Hopkins Hospital Bulletin, September, 1900.

animal experiments have been employed the descriptions are frequently so meagre as to leave the identity of the organism wholly in doubt. In France it is usually assumed without any discussion, even without any bacteriological examination, that *gangrene foudroyante* is malignant œdema (Pasteur's septicæmia). The only exception is that of Guillemot,<sup>1</sup> who found the bacillus *aërogenes capsulatus* in a case of gaseous gangrene, and who controverts the prevalent belief of authors who attribute this disease exclusively to Pasteur's vibrio. The same ignorance of the present status of this subject is still sometimes encountered in England, Germany and elsewhere. Nevertheless, the investigations of the last seven years, taken with those of E. Fraenkel, and soon followed by observations of myself and collaborators, have demonstrated that by far the most common and important specific cause of gaseous phlegmon or emphysematous gangrene is the bacillus *aërogenes capsulatus*."

Whether the bacillus of malignant œdema can produce an identical or similar anatomical and clinical affection in human beings, Welch regards as an unsettled question. He writes: "It is certainly remarkable, in view of current doctrines in text-books, that neither E. Fraenkel nor I, with our relatively large experience, nor, indeed, so far as I am aware, anyone who has made himself thoroughly acquainted with the bacillus *aërogenes capsulatus*, has encountered the existence of emphysematous gangrene in man caused by the bacillus of malignant œdema. The whole subject of human malignant œdema is one which needs thorough revision and investigation by more exact bacteriological methods than have yet been applied to it. In a case reported recently by Brabec<sup>2</sup> the identification of the malignant œdema bacillus seems satisfactory. Here there was an extensive bloody œdema without gas, so that the case was not one of emphysematous gangrene. On the other hand, the latest writers on the subject, Hämig and Silberschmidt,<sup>3</sup> bring no proof of any consequence that they were dealing, as they supposed, with the malignant œdema bacillus in two cases of *gangrene foudroyante*. There is a relatively small group of cases of gaseous phlegmon attributed by those reporting them either to the colon or the proteus bacillus. In most of these cases anaërobic culture methods were not employed. No one has succeeded in producing experimentally gaseous phlegmon with either of these bacilli, and I think there is good reason to be skeptical concerning their capacity to produce this disease, unless perhaps the bacillus coli may do so in diabetes. It is possible that some of those reporting the colon bacillus as the cause of emphysematous gangrene

<sup>1</sup> Compt. rend. de la Soc. de Biologie, 1898, x., s. v., p. 1017.

<sup>2</sup> Wiener klin. Rundschau, 1900, xiv., pp. 145 and 167.

<sup>3</sup> Correspondenzbl. f. Schw. Aerzte, 1900, xxx., p. 361.

may have confounded with it a facultative anaërobic bacillus which we have isolated from two cases of the disease and which has been studied in my laboratory by Dr. Lanier. It resembles in anaërobic cultures very closely the bacillus *aërogenes capsulatus*, but it is capable of aërobic growth also, and then the rods are thinner and more like the colon bacilli. It has the power of producing gas abundantly in the blood and tissues of rabbits killed a few minutes after intravenous injection—a power not possessed by genuine colon bacilli. I have already spoken of the importance of this test, which has been employed by none of the writers who have claimed to find colon bacilli as the cause of gaseous phlegmons. This bacillus (Lanier's), when virulent, is capable of causing the same spreading and fatal emphysematous necrosis in guinea-pigs and pigeons as is the bacillus *aërogenes capsulatus*."

Dr. Welch writes, further, that he has been accustomed to speak of this bacillus as the aërobic variety of the gas bacillus. He believes now, however, that it is identical with Sanfelice's<sup>1</sup> bacillus pseudo-œdematis maligni, with which he is inclined to identify Klein's<sup>2</sup> new "bacillus of malignant œdema."

Chavigny<sup>3</sup> has isolated apparently the same bacillus, which he, likewise, identified with Sanfelice's bacillus from a case of gaseous gangrene, and also calls attention to what Dr. Welch has just done, to the probability that others may have mistaken this bacillus for the colon. Dr. Welch further writes: "While, therefore, unwilling upon existing evidence to accept the colon bacillus as a demonstrated cause of gaseous gangrene (except, perhaps, of diabetes), I am of the opinion that the anaërobic bacillus, probably identical with Sanfelice's bacillus pseudo-œdematis maligni, is capable of producing this affection, but it is much less frequently concerned than the bacillus *aërogenes capsulatus*." I have quoted Dr. Welch almost *verbatim*, because it is important for all of us to have clearly stated by such an authority this opinion on the possibility of malignant œdema in human beings. For the bacteriological difference between the bacillus *aërogenes capsulatus* and the bacillus of malignant œdema I would refer those interested to the original article of Dr. Welch.

PROGNOSIS OF EMPHYSEMATOUS GANGRENE. Dr. Welch writes that he thinks the prognosis is more favorable to-day than before the antiseptic period. In his forty-six collected cases death took place in 59 per cent. In the cases observed and treated in the Johns Hopkins Hospital (ten in number) the fatality was but 50 per cent.; but of

<sup>1</sup> Ann. d'Inst. d'Igiene sper. d. R. Univ. di Roma, 1891, n. s., i., p. 365, and Zeit. f. Hyg., 1893, xiv., p. 352.

<sup>2</sup> Centralbl. f. Bakt., 1891. x., p. 186.

<sup>3</sup> Ann. de l'Inst. Pasteur, 1897, xi., p. 860.

these five deaths one was a gaseous phlegmon of the pelvis extending to the thigh (which was not admitted to the hospital until the tenth day of the disease). The second was a gaseous phlegmon of the abdominal wall, following removal of the appendix and complicated by peritonitis, and a third case died twenty-five days after the disappearance of the gaseous phlegmon from a late streptococcus infection. Of the two remaining cases, in one amputation was refused by the patient until the fourth day, when he was in a state of collapse; he died fifteen hours later. In the other case there was a compound fracture of the skull and both lower extremities, and the patient died thirty hours after the accident, having never regained consciousness.

Dr. Welch agrees with my conclusion in stating that when the disease is accessible to surgical treatment, and is uncomplicated by other grave conditions, and is promptly recognized and treated, prognosis is not very unfavorable.

CONCLUSION AS TO THE GAS BACILLUS INFECTION. Dr. Welch's observations demonstrate the wide distribution of the gas bacillus in the soil and in the dust of hospitals and perhaps other buildings. It is a common occurrence in the intestine, and it may be present if looked for in other parts of the body. Virulent gas bacillus infections are distinctly more common with us in Baltimore than tetanus infections, and stand next to streptococcus infections. Both the gas bacillus and the streptococcus infections are of such virulent character that to save your patient a very early treatment is demanded. For this reason the possibility of a virulent infection with the gas bacillus or the streptococcus should be borne in mind in every recent injury, especially bullet wounds and compound fractures, and especially in wounds in which there is great contusion. I would earnestly urge that cover-slips be made from the blood and tissues in all open recent wounds; that such cover-slips and cultures be made when the wound is first examined, before it is disinfected; it takes but a moment, and within the next forty-eight hours a second examination should be made if the wound has been left open. The slightest indication of fever, leucocytosis, or local symptoms should be followed at once by a bacteriological examination of the exudate in the injured part. Demonstration in the cover-slips of the characteristic bacillus or the characteristic chains of cocci should be followed at once by operative measures. I feel certain that in one of my own cases this routine procedure made us operate a number of hours earlier. The patient was admitted with a multiple duck-shot wound of the upper thigh. He was in splendid condition, and was taken to the ward at once. On pressure of the thigh first blood-stained serum exuded. Cover-slips made from this serum showed numerous bacilli morphologically like the gas bacillus. Deeper pressure brought out

frothy blood. The operation was performed at once. There were no local or general symptoms of infection of any high degree. If the patient had simply been placed in an antiseptic dressing and watched we feel certain that before there were sufficient signs, local or general, to urge the ordinary observer to examine the wound the infection would have extended so that amputation would have been indicated, and even this at so late a date might not have saved the patient. In all our cases the gas bacilli have been so numerous and of such characteristic morphological appearance that they have been recognized in cover-slips and a diagnosis made, even in those cases where gas was not present in the tissues. In every instance the cover-slip diagnosis was confirmed by careful bacteriological study.

#### **The Subcutaneous and Intravenous Serum Treatment of Tetanus.**

The most important contribution to the literature of this subject is a collective review by Dr. Frank Steuer,<sup>1</sup> March, 1900. Steuer has collected the entire literature (over 181 references), has tabulated the cases, and studied them with the greatest detail. The result is very disappointing. There is little to be said for the antitoxin treatment of tetanus after the disease has shown itself clinically. This, of course, is in conflict with the various individual reports that are getting into the literature from time to time. The explanation for this no doubt is that we do not know how to estimate the ordinary mortality for the individual cases. Steuer's investigations, however, almost conclusively prove that the problem of the antitoxin treatment of tetanus is far from being solved. We know that tetanus is a distinct infection. The bacillus is present in the wound, and in only a very few cases has it been found in the blood. The infection is due to the absorption of the toxins from the wound. These toxins are in the circulating blood, and are rapidly taken up by the cells in the brain and cord. There is always some time between the date of infection and the onset of the symptoms. Steuer has shown from the investigations of others that the antitoxin can affect only the toxin in the circulation, that it cannot affect the toxin already taken up by the nerve cells. So that in the human being, when one waits for the symptoms of tetanus, we can only counteract the toxin present in the circulating blood. We cannot affect that which is already absorbed and in some chemical combination with the protoplasm of the nerve cells.

Steuer goes carefully into the problems of the toxin and the antitoxin, which cannot be discussed here, because to make it clear would require too much space. The problem, however, is not yet a settled one,

<sup>1</sup> *Centralbl. f. die Grenzgebiete der Med. und Chir.*, 1900, Bd. iii., Nos. 5, 6, 7, 8, 9, 10, and 11.



although our knowledge of the different forms of immunity has increased greatly in the last few years.

**THE VARIETIES OF ANTITETANUS SERUM.** In commerce there are a number of different forms of serum which have been used in the treatment of tetanus, most of which are reliable: Behring's serum, made in Germany; Tizzoni's in Italy, and that of Roux, Villard and Pasteur in France; in England, from the British Institute of Preventive Medicine, and of Jenner; in America, that prepared by Parke, Davis & Co., of Detroit, and others.

**METHODS OF INJECTION.** The serum has been given subcutaneously and intravenously and also subdurally and intracerebrally. On the whole, the subcutaneous method is the best. The intravenous and the subdural and intracerebral seem to have given no better results, according to Steuer's studies, than the subcutaneous injections. Subcutaneous injections are unquestionably the simpler and safer. Injections of brain emulsions and the injections of certain antiseptic substances, such as carbolic acid and bichloride of mercury, have also been used, but according to Steuer the results are still uncertain.

**THE TOXIN AND THE ANTITOXIN.** Steuer writes that this investigation points to the fact that the tetanus toxin is actually able to act directly on the substance of the motor ganglion cells and to produce changes in them. These changes cannot be of a particularly grave character, as after-affections of healed tetanus are not usually observed. The communicated cases of post-tetanic paralysis are extremely rare. In regard to the antitoxin Steuer writes: "We may, therefore, positively say now that the neutralization of the toxin by the antitoxin takes place in a thoroughly mechanical manner; that the toxin is here not actually destroyed, but enters into loose chemical combination with the antitoxin, which is itself harmless. This combination, however, only takes place between the toxin in the circulating blood, and not with that already in chemical combination with the protoplasm of the nerve cells.

**PRESENT TREATMENT OF TETANUS IN MAN.** One should unquestionably use the antitoxin in a case of tetanus in man the moment the symptoms are recognized. We cannot hope to do much for the poison already absorbed and in combination with the nerve cells, but we can destroy that which is already present in the circulating blood, and we can destroy, if we continue the injections, any more tetanus toxins that may be absorbed from the wound. Therefore, the antitoxin treatment of tetanus would emphatically contraindicate amputations of limbs in order to remove the portal of infection, because the serum will neutralize the toxin absorbed later from the wound. It is only necessary in regard to the wound to thoroughly open and disinfect it, but ampu-

tations or any mutilating operations are unnecessary. This is a very important observation, for the moment that we begin our serum injections we can feel assured that the patient will only have to combat the poison already in chemical combination with the nerve cells. Steuer is very emphatic in saying that in addition to the serum treatment one should not neglect the older therapeutic agents: opium, which is best given in hypodermatic injections of morphine; chloral hydrate and bromide of potassium, which are better given by rectal injections, and chloroform anæsthesia when indicated.

**PREVENTIVE VACCINATION.** We have much to learn from the veterinary surgeons in the treatment of tetanus. Their results with the antitoxin treatment in animals, after the clinical symptoms of the disease have manifested themselves, have yielded practically the same results as in man; but the veterinary surgeons have introduced preventive vaccinations. In districts where tetanus is common, previous to the operation the animal is injected with tetanus serum, and in quite a large series of cases the results demonstrate without doubt the immunity which these injections give. There are either no symptoms whatever of tetanus or they are very slight, with rarely a fatal result.

Preventive vaccination in man should also be used. Tizzoni records two interesting cases. Both patients were infected with the tetanus toxin in his laboratory, and were immediately injected with his antitoxin. The first patient was a student, who infected the ends of several of his fingers with a highly virulent tetanus culture. The antitoxin was used three days afterward. The symptoms were but slight, and the student recovered. In the second case the antitoxin was used twenty-four hours afterward. At the end of thirteen days there were slight contractions of the muscles of the jaw and lower extremities, but these symptoms quickly disappeared. Tizzoni further reports protective vaccination in patients with extensive wounds which have been soiled with earth and in which it was thought that the chances of tetanus were great. In one, from the secretion of the wound, the tetanus bacillus was demonstrated bacteriologically. Neither this patient nor the others developed any symptoms of tetanus. Bazy has also used the preventive vaccination. He decided to immunize with the antitoxin all his surgical cases in which he thought the conditions for tetanus favorable, and he states that in all the vaccinated cases (twenty-three in number) no symptoms of tetanus developed, although in the previous year in similar cases he had observed four cases of tetanus. During the tetanus epidemic at the Bohemian obstetric clinic in Prague, lasting from November, 1897, to September, 1898, all antitoxic measures failed, and there were always new cases. Only after, beginning with October, the preventive vaccination was systematically used on every operated woman there

were no new cases, while in other clinics in Prague there occurred further cases during the following three months. The results at the German obstetric clinic there were completely analogous. From these experiments it would seem desirable for surgeons to inject with the antitoxin of tetanus all recent injuries in which the wound has been contaminated with earth, especially in those districts in which tetanus is common. The injection of the serum is harmless, while the probabilities of success of the preventive vaccination if the wound is infected with the tetanus bacillus is very large; in fact, almost positive.

There have been a few single cases reported where the prophylactic vaccination seems to have been a failure, even when it has been made immediately after the injury. The cause of this failure in these few cases still remains a mystery. Monad, Buschke, and Ranje report failures. There are but few observations which would allow us to estimate the length of time that the preventive injection of the serum gives immunity. Villard has an observation in which the immunity lasted from two to six weeks. Repeated injections, however, will extend the time. Beck, in his experiments on animals, states the time at about three weeks, while Tavel states that the immunity is from four to six weeks. The immunity, therefore, is only a matter of a few weeks, but there are no observations demonstrating that it is longer.

STEUER'S CONCLUSIONS. From this experience it is clear that the opinions of the serum therapy cannot incline one in favor of a positive curative effect of the serum.

1. In tetanus already broken out the curative serum has no longer any therapeutic effect on the present complex of symptoms, and is hardly able to prevent the appearance of new symptoms of the disease. It may be assumed that it prevents the toxin still circulating in the blood from developing injurious effects; but this brings no essential change in the general course of the disease, as its intensity probably depends on the quantity of toxin formed during the time of incubation, and which has probably begun its action. This is the result of theoretical discussion; from the failure of most experiments on animals; from the uniform statistical data; from the observation of the effect of the serum in single cases, and from the communication of almost all the veterinary surgeons.

2. Nor does the early injections of the serum—that is, within the first three days *after the onset of the disease*—give any distinctly better results.

3. No difference can be made out in the manner of action of the various antitoxins which have been used.

4. No injurious symptoms consequent to the application of the serum have been observed.

5. The results of the prophylactic vaccination in cases in which the

onset of tetanus is to be expected are very good in the timely application of the toxin.

There are, unquestionably, districts in this country in which prophylactic injections should be used in recent injuries. In the Johns Hopkins Hospital we have had eight cases of tetanus in ten years among about 30,000 patients, demonstrating that tetanus is uncommon in this district. The mortality of these cases has been about 45 per cent.—the mortality given by Steuer for the cases in which the antitoxin has been used. We have used the antitoxin in one case only; in this instance given intracerebrally. The patient died.

FIG. 22.



Dr. Osler's case of multiple gangrene in malarial fever.

**Multiple Gangrene in Malarial Fever Simulating Raynaud's Disease.** In the differential diagnosis of spontaneous gangrene the surgeon must constantly bear in mind the possibility of the multiple areas of gangrene being due to the malarial poisoning. A most interesting case has lately been reported by William Osler.<sup>1</sup> The lesions are beautifully illustrated in Figs. 22 to 26. Osler writes that we must distinguish three groups of multiple gangrene :

1. *Raynaud's Disease.* There have been previous well-marked vascular disturbances in the extremities—syncope, asphyxia, or hyperæmia.

<sup>1</sup> Johns Hopkins Hospital Bulletin, February, 1900, vol. xi., p. 41.

The gangrene is very often symmetrical ; is usually slight in extent ; limited to the fingers or toes, more rarely to the ear tips or nose.

FIG. 23.



FIG. 24.



Dr. Osler's case of multiple gangrene in malarial fever.

2. *Multiple Spontaneous Gangrene of the Limbs* in young or middle-aged persons without any obvious cause, mainly gangrene of one, two, or three extremities occurs. Many illustrations of this are reported in the literature.

FIG. 25.



FIG. 26.



Dr. Osler's case of multiple gangrene in malarial fever.

3. *Multiple Spontaneous Gangrene in Association with the Acute Infections.* In measles, typhoid fever, typhus fever, scarlet fever, diphtheria, and malaria local gangrene may occur. There are multiple patches not symmetrical, and the skin and adjacent tissues are more frequently affected than the extremities. While, of course, the phenomena of Raynaud's disease may occur as the sequence of any of the specific fevers, a large proportion of all the cases of local gangrene occurring during and after one of the fevers have nothing whatever to do with this affection. Osler further writes: "The relationship between malarial fever and Raynaud's disease is believed to be very close. Many references are given to cases (the majority from French sources) by Barlow in his article in Allbutt's *System*, and more fully by Monroe,<sup>1</sup> in his monograph. Altogether in the cases collected by Monroe there were only 8.3 per cent. with malarious antecedents." Osler has looked over his notes on cases of Raynaud's disease which he observed in Baltimore. They were nine in number, and in not a single case was he able to demonstrate malaria as an etiological factor, and so far as his observations have gone in a very large class of cases of malaria during the past ten years he has not observed a single instance of Raynaud's disease. The case reported by Osler is the first one observed in the Johns Hopkins Hospital. Multiple gangrene occurred in a case of æstivo-autumnal malaria. Similar cases occurring have been reported in the literature and are referred to by Monroe, but they are exceedingly rare. The case reported by Osler was first admitted to the surgical department of the Johns Hopkins Hospital, and I had the good fortune to see him. In the history of the multiple gangrene the preliminary stages generally observed in Raynaud's disease were absent, and although the local appearance of the gangrene itself and its somewhat symmetrical distribution suggested the possibility of Raynaud's disease, yet the absence of any previous manifestation of syncope, asphyxia, or hyperæmia made the diagnosis doubtful. The possibility of its relationship to malaria was thought of and the patient transferred to the medical side.

The clinical summary of this case is as follows: Malaria when six years old; typhoid fever twice, last attack four months before onset of present illness. Illness in the middle of October (one month before admission), supposed to be influenza, but probably malaria. On November 2d, twenty-seven days before admission, onset of spots of gangrene in legs, parts of hand; rapid extension—condition shown in illustration. Patient's complexion was muddy; spleen was enlarged; the blood showed very many æstivo-autumnal organisms; temperature

<sup>1</sup> Glasgow, James Maclehose & Son, 1899.

slightly elevated at first, subsequently no fever. Cultures from the blood negative; no leucocytosis. Treatment: Quinine in full doses, followed by rapid recovery.

The history of the onset of the gangrene was as follows: About the middle of October, six weeks before admission to the hospital, the patient had an attack of illness of two weeks' duration, which was called influenza; there were no distinct chills or fever. On November 2d, after the patient had been up and about a few days, and twenty-seven days before he was admitted to the hospital, he noticed blebs, about one-half inch in diameter, on both hands, which were slightly swollen. Previous to this nothing had been noticed in the skin in any part of the body. On the next day a mottled area appeared on the instep of the left foot, which looked like a bruise; then similar ones appeared on the buttocks and dorsum of the right foot; later other spots. Both hands and feet became swollen; the blebs broke and discharged a dark fluid. The skin around the infected area was red; no itching; some pain at night. There has been no redness, swelling, or bluishness of the fingers or toes, nor has there been numbness or tingling. Dr. Fletcher, resident physician, made the following note: "Patient is sallow, and the entire skin is pigmented, most marked about the nipple and umbilicus; no pigmentation of the mucous membranes. On the dorsum of the hand just behind the knuckles there were four whitish scars, the result of healing vesicles. Over the ring, middle, and little fingers there is a bluish-yellow discoloration of the skin, which is gradually peeling off where the blebs are healing. On the palmar surface of the fingers the skin is raised in blebs. The skin has a brownish-yellow color, and over the ring finger is quite gangrenous, and the subcutaneous tissue is involved. Thumb and index finger are not involved. *Right hand.* Dorsum of this hand is unaffected. On the dorsal surface of the first and second interphalangeal joints of the index, middle, and ring fingers the skin is thickened, brownish in color, but no vesicles. Over the hypothenar eminences on the palm is a large area measuring 5 x 6 cm., in which the skin is loosened from the subcutaneous tissue, markedly discolored, and at one point a serous fluid is exuding. The palmar surface of all four fingers show a gangrenous condition of the skin, with vesiculation and oozing of a fluid most extensive on the ring finger, where the process invades the palm of the hand. *Right foot.* Over the dorsum of the foot below the ankle is an area 5 x 3 cm. in which the skin is gangrenous and exceedingly black. Sloughs still adherent to adjacent tissue surrounding the skin, slightly pigmented. Over the heel there is an area of brown, discolored, thickened skin, measuring 5 x 6 cm. This area is sensitive to the touch. *Left foot.* Below the external malleolus is an area 5 x 3 cm. of gangrenous, sloughing, black skin. *Left buttock.* Just over the spine at



the junction of the dorsal and lumbar regions there is a patch of dry, gangrenous skin, 1.5 x 2 cm. Over the left gluteal region there is an irregular gangrenous patch, quite dry, measuring 4.5 x 2 cm., slightly sensitive to pressure. Over the lower part of the occiput on each side there are two areas in which the scalp has a gangrenous appearance. There is slight oozing of fluid, causing matting of the hair."

This observation is a very interesting and important one, and the possibility of multiple gangrene being due to malarial fever should be constantly borne in mind, not only in malarious districts, but in patients returning from any country in which there is a possibility of malarial infection. It should be borne in mind, especially by the army and navy surgeons, and perhaps the records of the late war would show more instances of this character. This patient was with the volunteer army in the South, and in the previous August had had an attack of typhoid fever.

## FRACTURES AT THE ELBOW-JOINT.

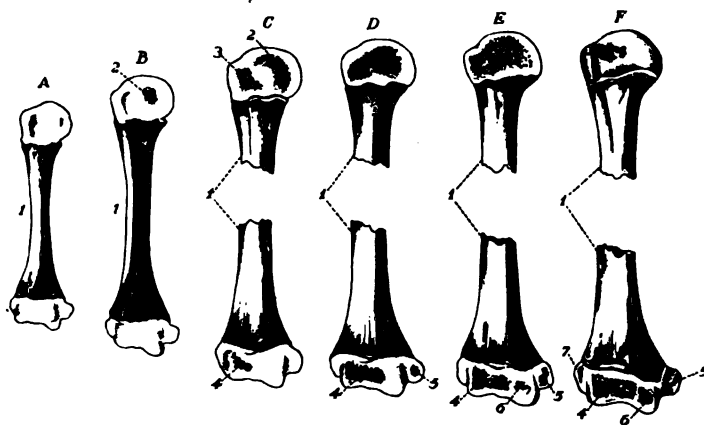
**Epiphyseal Separations at the Lower End of the Humerus.** Although we have a number of recent text-books, both in English and German, on fractures, in none of them are the X-ray photographs of the different forms of epiphyseal separation of the lower end of the humerus complete. For this reason I feel that a review of Wolff's<sup>1</sup> most complete article will be very welcome to those interested in the subject. Wolff's article (about 155 pages) has thirty-two clear X-ray photographs. He considered practically all the possible epiphyseal separations. The X-ray photographs are from his own observations. I shall here only consider those at the elbow-joint, because this part of his article is the most complete.

**THE EPIPHYSES AT THE LOWER END OF THE HUMERUS.** Before one can understand these epiphyseal separations one should familiarize one's self with the development of the lower end of the humerus, and I reproduce from Quain's *Anatomy* (Fig. 27). It is seen from this figure that the lower end of the humerus develops from four separate nuclei. The first to appear is that at the capitulum (Wolff calls it *rotula*), in the third year; the next the internal epicondyle, in the fifth year. The trochlea, according to Quain, in the eleventh and twelfth years; according to Wolff, in the eighth year. That of the external epicondyle, according to Quain, in the thirteenth or fourteenth year; according to Wolff, in the eighth year. Wolff's X-ray photographs demonstrate that

<sup>1</sup> Concerning Traumatic Epiphyseal Separation. Deut. Zeit. f. Chir., January, 1900, Bd. liv., Heft 3 and 4, p. 287.

he is correct. In addition to this, it must be remembered always that at the eighth year the external condyle and capitellum unite, so that after the eighth year one cannot have an epiphyseal separation of the external epicondyle alone. There must be either a fracture or a separation with the capitellum. At about the thirteenth year the already united external epicondyle and capitellum unite with the trochlea, so that after the thirteenth year we can only have the separation of these three nuclei together. These three nuclei unite with the diaphysis between the sixteenth and seventeenth years. The nucleus of the internal epicondyle

FIG. 27.



Epiphyses at lower end of humerus.

4, capitellum (rotula); 5, internal epicondyle; 6, trochlea; 7, external epicondyle.

remains as a distinct epiphysis, and does not unite with the diaphysis and the remainder of the epiphysis until the eighteenth or nineteenth year.

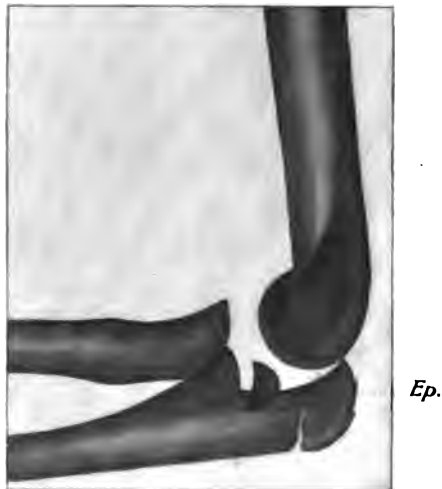
**THE X-RAY SHADOW OF THE LOWER END OF THE HUMERUS.** As bone and not cartilage produces a shadow in the Röntgen picture, we can readily see that up to the third year X-ray photography is no help in the diagnosis of fractures of the lower epiphysis of the humerus. After the third year only the capitellum (rotula) is projected; but if we study the normal relation of this shadow to the shaft we can tell by its displacement what has taken place with the remainder of the epiphysis. After the eighth year we may have a displacement of the capitellum and external epicondyle together; but after the thirteenth year there are only two possible epiphyseal separations—that of the three coalesced nuclei (external epicondyle, capitellum, and trochlea) and the internal epicondyle. However, in the sixteenth or seventeenth

year, and up to the eighteenth or nineteenth, epiphyseal separation of the internal epicondyle only is possible. These fractures during the period of growth are very common. Between the ages of one and eighteen years in 109 fractures, 37, or 33 per cent., occurred at the elbow. Of these 37, 7 were epiphyseal separations, so that up to the eighteenth year when one has a fracture in the neighborhood of the elbow-joint the possibilities of its being epiphyseal are one in four (about 25 per cent.). After the eighteenth year a separation of the capitellum and external epicondyle is called a fracture of the external epicondyle in adults, while separation of the trochlea and internal condyle is called a fracture of the internal condyle in adults. Isolated separation of the rotula and trochlea together are rare. Boydenhauer demonstrated it

FIG. 28.



FIG. 29.



anatomically in one case. Wolff has observed no cases, although he has observed separation of the rotula, trochlea, and external epicondyle together in six cases. , Wolff's cases of epiphyseal separation :

(1) Separation of the epicondyles, six times ; (2) separation of all the epiphyses together, six times ; (3) trochlea with external epicondyle, once ; (4) rotula with internal epicondyle, once. In this case it was associated with a fracture of the diaphysis.

These epiphyseal separations of the lower end of the humerus similar to fracture in the adults are due either to direct trauma of the elbow or indirect from falling on the palm of the hand.

*Epiphyseal Separation of the Epicondyles.* These two X-ray photographs<sup>1</sup> (Cases I. and II., Figs. 28 and 29) represent epiphyseal separa-

<sup>1</sup> Deut. Zeit. f. Chir., Bd. liv., Heft 3 and 4, p. 290.

tions of the internal epicondyle (*Ep.*). In Case I. (Fig. 28) the epiphysis is simply separated outward; in Case II. (Fig. 29) one sees that the epiphysis is dislocated downward and forward. In both the injury was by direct force—falling on the elbow when the forearm was flexed. In both Wolff was able to replace the fragment; there appeared to be bony union in three weeks, and there was perfect joint function. In Cases III. and IV., Figs. 30 and 31,<sup>1</sup> the fracture was due to a tear by indirect force from falling on the extended hand. In both we see that the internal epicondyle is separated (*a*), also the separa-

FIG. 30.

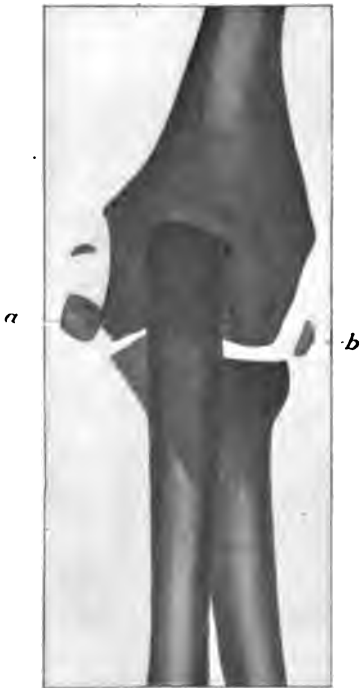


FIG. 31.



*a*, internal condyle; *b*, external epicondyle. *a*, internal condyle; *b*, external epicondyle.

tion of the external epicondyle (*b*); but as these patients were respectively fourteen and sixteen years of age, and as we know that the external epicondyle is united by bony union with the capitellum after the eighth year, this is not a true epiphyseal separation, but a fracture. Figs. 30 and 31 are, therefore, good illustrations of the appearance of the elbow-joint at the ages of fourteen and sixteen years respectively. As we can hardly see the line of demarcation between the epiphysis and

<sup>1</sup> Deut. Zeit. f. Chir., Bd. liv., Heft 3 and 4, p. 291.

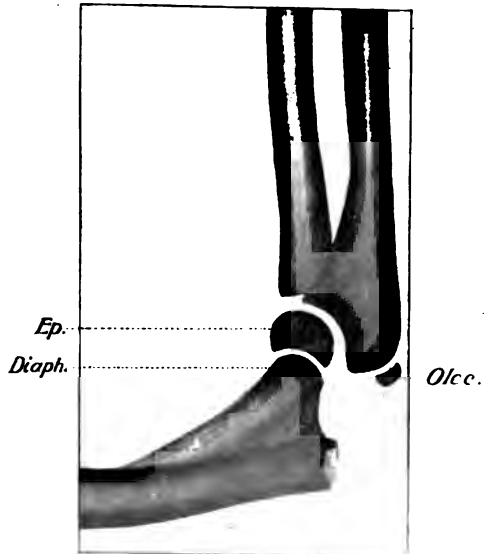
the diaphysis, we would infer that ossification between the capitellum and trochlea and the shaft is almost complete. This usually takes place in the sixteenth or seventeenth years. The result in Case III. was bony union, but in Case IV. there was a pseudarthrosis, and in this case six years later it was necessary to remove the fragment of the internal condyle, because it was producing pressure on the ulnar nerve. The joint and function in both cases was excellent. In Case V. (Fig. 32) there was a separation of the internal epicondyle (*a*) downward for some distance. It was impossible to replace this fragment; there was

FIG. 32.



*a*, internal epicondyle; *b*, external epicondyle; *c*, capitellum; *d*, trochlea.

FIG. 33.



*Ep.*, epiphysis of humerus; *Diaph.*, diaphysis; *Olec.*, olecranon epiphysis.

a pseudarthrosis, but not associated with any injury to the nerve. The ultimate result has been a perfect one. Wolff does not tell us the age of the patient in Fig. 32, but we clearly see the epiphysis of the external epicondyle (*b*) not yet united to the distinct epiphysis of the capitellum (*c*), so that we know that the patient must have been under eight years of age. The smaller epiphysis of the trochlea (*d*) is also shown. Only the internal epicondyle (*a*) is out of place. The diagnosis of epiphyseal separation is not especially difficult, any more than a diagnosis of separation of either condyle after ossification. There is always some swell-

ing of the joint, generally joint effusion, as the separation is intracapsular. One usually feels the separated epicondyle, which in the majority of cases is dislocated. If the dislocation is not marked bony union usually takes place in fourteen days; if a dislocation, however, is extreme, one is seldom able to replace the fragment, and there is pseudarthrosis. In the majority of cases, however, this produces no functionally bad result; but now and then, on account of pressure on the ulnar nerve by the epicondyle, the fragment must be removed. Its removal, however, does not affect the function of the elbow-joint.

*Partial Separation of all Four Epiphyses.* It is not an infrequent accident to have a partial separation of the lower apophysis of the humerus. It differs only from a complete epiphyseal separation in degree, and is produced by the same trauma. The arm is generally flexed at rather an obtuse angle in slight pronation; very little active motion possible; some passive motion. There is a good deal of effusion, as the injury is intracapsular, and one seldom gets crepitus. The diagnosis must be based on clinical signs. The X-ray photograph frequently is of little value, because up to the third year none of the nuclei have ossified; and from the third to the eighth year we have nothing but the capitellum and the internal epicondyle. After the fifteenth year, as stated before, the capitellum and trochlea are united and show in the X-ray photograph; but a line between these epiphyses and the diaphysis is a broad one, and only by comparison with the normal side can one make out by the separation that there is no dislocation. Reduction in these cases is simple; healing is rapid, generally in three weeks, and the prognosis is good.

EPIPHYSEAL SEPARATION OF THE LOWER APOPHYSIS OF THE HUMERUS, WITH DISLOCATION. This is a more serious accident, as the dislocation may be marked. Reduction is more difficult and good results less frequent. This epiphyseal separation corresponds somewhat to the supracondyloid fracture, which may occur in youth as well as in the adult, although in the youthful individual the epiphyseal separation is more common. The position of the fragment in either the fracture or the epiphyseal separation depends upon the direction of the force.

If the fall is on the elbow the lower fragment is *forward* and the upper fragment *backward*, and we get a flexion fracture of the diaphysis, the fragments forming an angle with each other, as shown in Fig. 33. In this case the line of fracture is above the epiphysis, and the epiphysis with the lower end of the diaphysis is dislocated forward, while the shaft is back and the two form an acute angle. In Fig. 34 the line of fracture is the same—supracondyloid—and we have an open angle, but the fragments are not dislocated and there is much less deformity. In this

case one sees the epiphysis in place. These are examples of supracondyloid fractures in children.

When the patient falls on the extended forearm on the palm of the hand the bones of the forearm are driven against the lower end of the humerus, and we get either supracondyloid fracture or an epiphyseal separation. In both cases the lower fragment goes backward instead of forward, while the upper fragment projects forward instead of backward, and the deformity is an angle of the opposite direction, and is called an extension fracture. This is well illustrated in Figs. 35, 36, and 37.

FIG. 34.

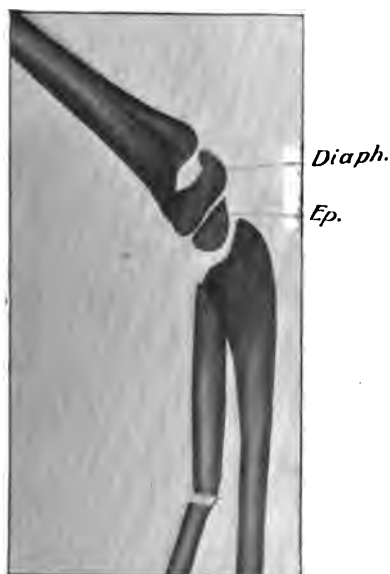
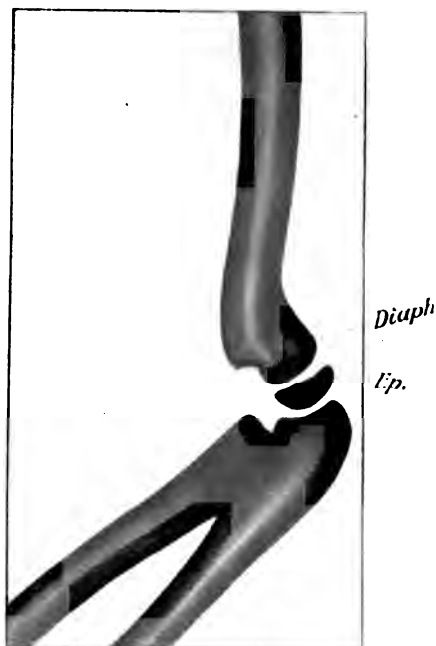


FIG. 35.



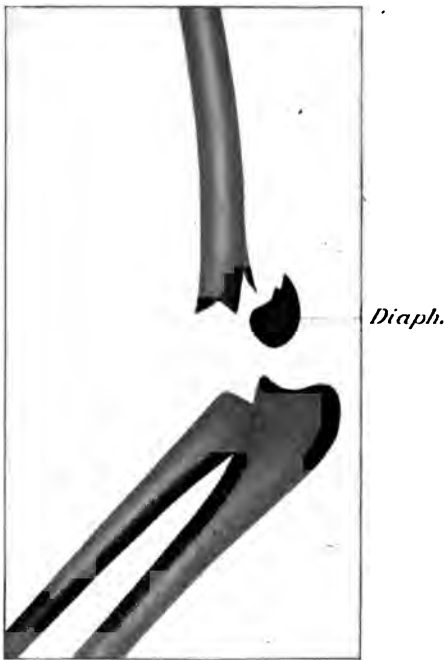
*Ep.*, epiphysis of humerus; *Diaph.*, diaphysis.

*Ep.*, epiphysis of humerus; *Diaph.*, diaphysis.

Fig. 35 is an X-ray photograph of a boy, aged fourteen years. Here we see the apophysis dislocated backward with a small piece of the diaphysis. At this age three of the nuclei have coalesced; the internal epicondyle is not shown, the picture being a lateral view. In Figs. 36 and 37 the epiphysis is not shown, and what we see is the fragment of the lower end of the shaft dislocated posteriorly. The patients were children, aged three and four years. Even the beginning nucleus of the capitellum is not seen. Comparing these two photographs with Figs. 34 and 35, you can see that there is a distinctly wider space be-

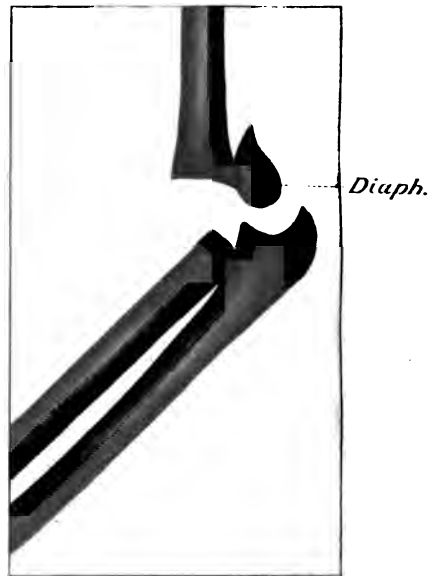
tween the lower end of the diaphysis and the ulnar bone. The force which produces an epiphyseal separation instead of supracondyloid fracture may also, from its direction, produce, in addition to the anterior-posterior dislocation, a lateral displacement of the lower fragment. Thus, if the force is from the posterior and out, the epiphysis goes forward and in, while if it is from the posterior and in, the epiphysis goes forward and out. The dislocation, however, is never purely lateral. This injury occurs frequently from a fall on the elbow, although it has been observed from a fall on the hand. The latter injury in children

FIG. 36.



Diaph., diaphysis.

FIG. 37.



Diaph., diaphysis.

is more apt to produce a dislocation. The X-ray photograph, as stated before, in these cases does not always help us, and is difficult to interpret, and we frequently must depend more on the clinical signs, especially under narcosis. For example, Fig. 38 is a difficult one to interpret. The clinical diagnosis is a separation of the lower epiphysis (the lower fragment being forward) in a child, aged four years. The only epiphysis seen here is that of the capitellum, which appears at the end of three years; but comparing it with a normal one it will be noticed that the shadow is dislocated to the medial side from  $\frac{1}{2}$  to  $\frac{3}{4}$  cm., showing that there is a lateral dislocation of the epiphysis, and indicating with-

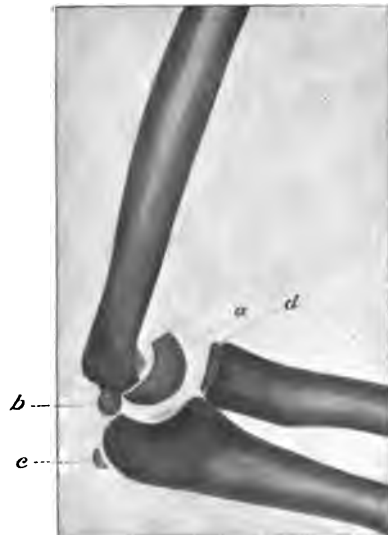


out much doubt an epiphyseal separation. In Fig. 39 the diagnosis from the X-ray photograph is clearer than in Fig. 38. Here we have an epiphyseal separation in a boy, aged fourteen years. At this age we know that the rotula, trochlea, and external epicondyle have ossified, and this is shown in the fragment which is dislocated forward. The small, round shadow just below the shaft of the humerus is that of the internal epicondyle, which does not become ossified until the eighteenth year. In two other cases the clinical signs were similar to these cases,

FIG. 38.

*Cap.*, capitellum.

FIG. 39.



*a*, united epiphysis of capitellum, trochlea and external epicondyle; *b*, internal epicondyle; *c*, olecranon; *d*, head of radius.

but as the children were under three years of age the Röntgen picture threw no light to confirm the diagnosis.

I have reviewed this article chiefly to produce these most instructive X-ray photographs, but I am surprised to find that Wolff believes that all fractures at the lower end of the humerus or epiphyseal separations are best treated with extension. I think that American surgeons will take exception to this. It seems to be the consensus of opinion in this country that fractures at the elbow-joint are best treated in the completely flexed position, the entire arm included with the body in the plaster dressing in this position.<sup>1</sup> Our experience at the Johns Hop-

<sup>1</sup> See Scudder on Fractures.

kins Hospital, both in the dispensary and in the house service, has been most satisfactory since we have used this position of complete flexion in treatment of fractures of the lower end of the humerus and at the elbow-joint, except, of course, fractures of the olecranon.

### **COXA VARA (CURVATURE OF THE NECK OF THE FEMUR).**

This interesting disease, the study of which has thrown so much more light on the conditions of the hip-joint, was pretty thoroughly discussed in *PROGRESSIVE MEDICINE* for December, 1899. In the past year nothing especially new has been added, but many of the observations have been confirmed; the most important is that of Sprengel in regard to traumatic coxa vara. Sudeck's theory in regard to the crest has been questioned by Bähr. The good results from operative and non-operative treatment of cases properly selected are increasing, and the knowledge of the disease has greatly increased, and with the aid of the X-ray and the exploratory incision differential diagnosis of conditions of the hip have been put on a more scientific basis.

**Coxa Vara Traumatica Infantum.** Sprengel, who was first to call attention to the difference between coxa vara as described by Müller and Hofmeister and that observed by himself and Kocher, in which latter instance the curvature of the neck of the femur was due to a separation at the epiphyseal head, recorded no positive cases in which it had occurred in infants, although he expresses the opinion that the majority of cases of fracture of the neck of the femur were not in the neck, as advocated by Whitman, but in the epiphyseal line.

Joachimsthal<sup>1</sup> reports a case. The patient was a girl, aged five and a half years. She had always been in good health, and there was no history of and no present evidence of rhachitis. Seven months previous to her admission to the clinic there had been a very slight trauma, after which the child complained of pain in the hip, but continued to walk. At the end of two days the pain disappeared, but the limp continued. On examination one finds 1.5 cm. shortening between the trochanter and the anterior iliac spine. There is some atrophy of the muscles of the right thigh, but very little, if any, restriction of motion at the hip, except in abduction. The X-ray photograph (Fig. 40) shows a definite separation between the head and the neck of the femur. In this case we have the ordinary history so common to tuberculosis of the hip. The deformity, however, would be a rare one for tuberculosis at so early a period, yet not an impossible one. In this instance the only deformity was elevation of the trochanter and restriction of the abduc-

<sup>1</sup> Arch. f. klin. Chir., 1899, Bd. lx., Heft 1, p. 71.

tion (Hofmeister's<sup>1</sup> Group I.). There was no note that the foot was rotated out or that there was adduction. I should judge, however, from the measurements that there was slight adduction, because the real shortening between the trochanter and the anterior iliac spine was 1.5 cm., while the measured shortening between the anterior iliac spine and the external malleolus was but 0.5 cm. We know that adduction gives an apparent shortening, but measured, lengthening between these two points. This is not noted by Joachimsthal. The diagnosis in this

FIG. 40.



Joachimsthal's case of traumatic coxa vara in a child five and a half years old.

case, of course, has been made only by the X-ray photograph; but our experience in X-ray photographs, especially that of Rammstedt (to be considered later), which has been confirmed by operative interference, makes the diagnosis pretty certain. The cases collected by Sprengel<sup>2</sup> were all over fifteen years of age. Beside Joachimsthal's case there is so far in the literature but one other in a child under ten years of age, that reported by Kermisson in a child aged seven years; the diagnosis was confirmed by an X-ray photograph.<sup>3</sup> Joachimsthal agrees with

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1899, p. 252.

<sup>2</sup> Ibid., p. 256.

<sup>3</sup> I have just observed a case similar to Kermisson and Joachimsthal, in a boy ten years of age, confirmed by an X-ray photograph.

Sprenkel's conclusions in that the observations which have been confirmed by the X-ray or exploratory operation should influence us in believing that perhaps the majority of fractures in this locality, occurring in young adults especially, and even in children, are situated not in the neck, but in the line of the epiphysis, between the head and the neck. Royal Whitman,<sup>1</sup> of New York, does not agree with Sprenkel in regard to the position of the fracture of the neck of the femur in children or even in young adults. Dr. Whitman states that since 1890 he has observed eighteen cases of fracture of the neck of the femur in children, and since 1897 he has confirmed his diagnosis by the Röntgen picture. During the present year he has been able to get one specimen. Of the 18 cases 8 were males and 10 females. Two patients were between two and three years of age; 7 between three and six years; 7 between six and nine years. Therefore, sixteen cases were under ten years of age, a very interesting and remarkable group. Two were sixteen years of age. In all of Whitman's cases there was considerable trauma, much more marked than in Joachimsthal's, all the children falling from a considerable height. In only one case was the history of trauma indefinite. He states that the physical signs in fractured neck of the femur in childhood are as follows: After the accident there is actual shortening, seen by the elevation of the trochanter, which is usually prominent. There is outward rotation of the leg. For a number of weeks or months after the injury there may be discomfort on manipulation and muscular spasm, some restriction of motion; but when repair is complete the range of motion is but slightly limited in extreme abduction, flexion, and inward rotation, and a slight limp is the only symptom that is apparent. These symptoms just described by Whitman are the clinical picture of a healed traumatic coxa vara. Whitman goes on to say that in his experience fracture of the neck of the femur is not as rare an injury as the majority of text-books and authorities would make us infer, nor is it always followed by immediate or persistent disability. In many instances the patients are able to walk within a few days after the accident. In such instances it is to be inferred that the separation of the fragments is incomplete or the fracturing is rather a bending. In these instances it is frequently the case that the early diagnosis is not made; but the persistent limp, accompanied by pain, may be mistaken for tuberculosis of the hip. In Whitman's patients four were seen within the first month after the accident; seven within two months; five within six months, and two within one or more years after the injury. Differing from older people, in children the period of disability is short, and the immediate result is practically a perfect functional

<sup>1</sup> *Annals of Surgery*, February, 1900, vol. xxxi., p. 145.

recovery ; but as the neck of the femur in its new position is subject to greater strain, a gradual exaggeration of the depression, with its attendant symptoms of actual and apparent shortening, limp, and disability, is extremely probable—the picture of coxa vara traumatica infantum. Whitman's clinical picture and result correspond to the observations of others ; but he is of the opinion that in the majority of cases the fracture is situated in the neck and not at the epiphysis. He brings for-

FIG. 41.



Bolton's case of fracture of the neck of the femur in a child.

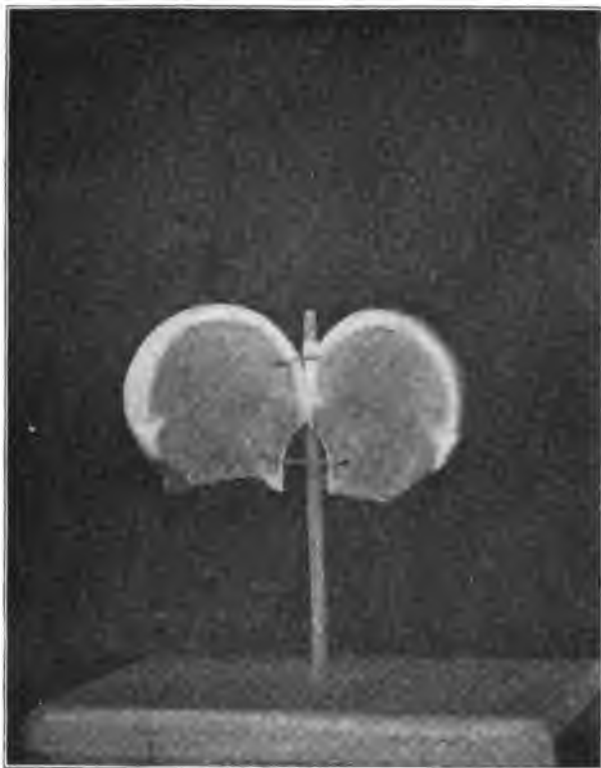
ward but one specimen, however, as an anatomical proof—a patient of Dr. Bolton<sup>1</sup> (Figs. 41 and 42). This, however, is the only anatomical specimen that Dr. Whitman has to prove his point. Dr. T. H. Myers, of New York, and Dr. C. L. Starr, of Toronto, showed before the American Orthopedic Association two anatomical specimens demonstrating

<sup>1</sup> *Annals of Surgery*, February, 1900, vol. xxxi.

fracture of the neck of the femur in young children obtained at autopsy.<sup>1</sup>

Whitman's second case, shown in Fig. 43, is a clear picture of separation at the epiphysis between the head and neck, and is so reported

FIG. 42.



Section of the same specimen, showing that the fracture is not in the epiphyseal cartilage.

by him. In view of the observations of Sprengel, Kocher, Joachimsthal, Rammstedt, and my own, in which either by X-ray or anatomical specimen the fracture has been demonstrated to be between the head

<sup>1</sup> Starr's case (Transactions of the American Orthopedic Association, 1899, vol. xii., p. 13) was first considered by him from the clinical symptoms as separation of the epiphysis. The child, however, died of diphtheria. At the autopsy a fracture was found in the neck just beyond the junction with the head. The child was three years old, and six weeks previously had fallen from a chair, following which there was a limp. No treatment had been instituted and the child had been allowed to walk. Starr was of the opinion that at the first there may have been an impaction, but later, due to walking, fragments had been displaced. Myers' case I cannot find.

and the neck in the epiphyseal line, and not in the neck itself, it would appear there is further anatomical and X-ray evidence that in children and in young adults, especially in the latter, the position of the frac-

FIG. 43.



Whitman's case of epiphyseal separation of the neck of the femur.

ture is in the epiphyseal line. Whitman's observations, however, are very important, and demonstrate that we may have a clinical picture of coxa vara in which the fracture is at the neck of the femur and not at the epiphysis.

Wolff,<sup>1</sup> in an article on "Traumatic Separation of the Epiphysis," states that fracture of the infantile femoral neck does occur, but is a great rarity. It has been observed once by Bruns in 189 cases. This is explained by the anatomical fact that the neck of the femur in youthful individuals is elastic, and the arrangement of these lamellæ are well adapted to resist force, while in the old the bone is not only brittle, but the lamellar arches are broken by the marrow cavities and the angle of the neck is decreased. Wolff has observed two cases; both were due to direct force on the trochanter; both were epiphyseal separation. The first case was not confirmed positively by the X-ray photograph, because in 1897 the development of the X-ray photography of the hip-joint was not such as it is to-day. The second case was completely confirmed by the X-ray. One case was aged eighteen months, and was observed fourteen days after the injury. The result was excellent with simple extension treatment. A second case was not seen until some weeks later, when there was a good deal of callous formation. The extension reduced the shortening somewhat, but deformity persisted. Wolff, therefore, agrees in his observation with Sprengel and Joachimsthal.

**Fracture of the Neck of the Femur in Infants.** Scudder,<sup>2</sup> of Boston, in his most recent work on fractures, agrees with Whitman, that the fracture is generally in the neck and not in the epiphysis. He quotes Bolton's, Myers', and Starr's cases, but has none of his own. He does not mention the recent literature just quoted, but confirms the important observation just spoken of, that such a fracture in old age is followed usually by complete disability, which is frequently overlooked in the child and treated for a contusion or sprain of the hip. This diagnosis is frequently confirmed, because the immediate result, even without treatment, is fairly good; but the ultimate result after several months or years in many cases is disastrous, due to the gradual bending of the neck of the femur. This late result of fracture in childhood resembles "hip disease" in the limp, slight pain, shortening, deformity, and limitation of motion, and it is most important not to confound the two conditions.

Stimson,<sup>3</sup> in the most recent edition of his book, speaks but briefly of separation of the epiphysis between the head and neck of the femur. He states that this epiphyseal separation has been demonstrated by specimens in a few cases and suspected in a large number in which the fracture has occurred in the young. Stimson, however, believes that it is much rarer than fracture of the neck at a corresponding age. He

<sup>1</sup> Deutsche Zeit. f. Chir., January, 1900, Bd. liv., Heft 3 and 4, p. 308.

<sup>2</sup> The Treatment of Fractures, Philadelphia, 1900.

<sup>3</sup> A Practical Treatise on Fractures and Dislocations, Philadelphia, 1899, p. 310.



refers to Bousseau's<sup>1</sup> case, in which at autopsy the fracture was demonstrated at the epiphyseal line. He refers also to Kocher's two cases: one a girl, aged sixteen years; the second a girl, aged ten years. Both of Kocher's cases were confirmed by excision of the specimen.<sup>2</sup> Here we see in the most recent and best American text-books on fractures that little space is given to this most important subject—the epiphyseal fractures of the upper end of the femur. Even Helferick,<sup>3</sup> in his most recent text-book on fractures, states that traumatic separation of the epiphysis of the head of the femur is an extraordinarily rare injury, and dismisses the subject in a few lines.

FIG. 44.



**Coxa Vara Traumatica Adolescentium.** Conrad Rammstedt,<sup>4</sup> of Halle, publishes the most interesting and instructive article in confirmation of Sprengel's work on traumatic coxa vara. Of his eight cases the X-ray in every case demonstrated that the fracture was at the epiphyseal line between the head and neck. In four cases the X-ray diagnosis was confirmed by operation. In his review he has considered the previous literature carefully. A short review, and

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1899, p. 259.

<sup>2</sup> Ibid.

<sup>3</sup> On Fractures and Dislocations. Translated by J. Hutchinson, Jr., London, 1899.

<sup>4</sup> Arch. f. klin. Chir., 1900, Bd. lxi., Heft 3, p. 559.

especially the illustrations, of his eight cases will be the most instructive method to aid us in the proper diagnosis and treatment. (These X-ray photographs are the best and most complete yet published.)

Case I. This patient, aged twelve years, gave a history of direct trauma nine years previous to admission to the clinic. (See Fig. 44.) For fourteen days after the injury the child rested in bed. After that time he got up and walked. Since then, however, there has been a limp and distinct retardation in growth. The accident, therefore, took place at three years of age, and is another observation of epiphyseal separation in children. The usual deformity of coxa vara was present. In addition to the real shortening there was 2 cm. shortening between the trochanter and external malleolus, due to retardation of growth in the bone. Motions of the hip were free except abduction and internal rotation. The X-ray photograph shows the healed fracture at the epiphysis; the head is dislocated downward and has partly left the acetabular cavity. The fractured end of the neck rests against the upper end of the acetabular cavity and bears the weight of the body. As the functional use was good there were no indications for operative or other treatment. This patient confirms Whitman's statement in regard to good function, even when there is deformity from dislocation of the fragments.

Case II. This patient was fifteen years of age. (See Fig. 45.) Two months previously there had been direct trauma on the trochanter, and following this there was a loss of function and swelling. The patient was out of bed in fourteen days, since which time he has walked with a limp and used two canes. The examination demonstrated the usual deformity and shortening of 4 cm. There was a slight degree of restriction of motion in all directions, except abduction, which was impossible. The trochanter was very prominent. The X-ray photograph shows the typical deformity, with a dislocated head and the neck resting against the upper rim of the acetabulum. In this case the operation consisted of excision of the head of the femur and the implantation of the rounded neck in the acetabular cavity. The wound healed *per primam*. The result has been slight increased mobility, less shortening, due to the corrected position from adduction to abduction, and no pain.

Case III. This patient was thirty-seven years of age. The trauma took place nineteen years ago, at eighteen years of age; it was directly on the trochanter. The patient, however, was able to get up and walk home, although with pain in the hip and a limp. He stayed in bed but a day, although he did not walk without a cane for three months; since then he has been able to do his work, although on account of the shortened leg he walks with a limp. He came to the clinic because of second slight trauma, and Rammstedt thinks more on account of a desire

to get an accident fee from a society than from any increase of the trouble in his hip. The examination showed the typical deformity. In addition, when the limb was moved there was slight crepitation, and the X-ray photograph showed, in addition to the fracture at the epiphyseal line, changes in the joint surfaces due to arthritis deformans, which, according to Kredal and others, is present in these cases of long duration.<sup>1</sup> I have had a similar observation. The operation in this patient consisted of a resection of the head and part of the neck. The head was small; it was dislocated downward, and rested over the

FIG. 45.



neck like a mushroom (similar to Kocher's and Sprengel's specimens). This specimen is another confirmation of Sprengel's view and against that of Whitman. It is important also to notice here the change in the head and the presence of a chronic arthritis.

Case IV. This patient was seventeen years of age, and the observation is an interesting one, because it was observed four days after the trauma, and *abduction* instead of *adduction* was present. (Hofmeister and others have noted *abduction*. I have seen one case.) The trauma

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1899.

was a direct one ; there was immediate pain and loss of function. The deformity noted four days later was outward rotation, flexion, and *abduction*, with 2.5 cm. shortening between the trochanter and anterior iliac spine. The trochanter was prominent ; all motions were painful, the hip being fixed by muscle spasm. Under ether, the muscles being relaxed, there was increased motion, but no distinct crepitus. The X-ray photograph (Fig. 46) shows that the line of fracture is at the epiphysis, and one sees clearly ragged edges. The treatment was extension, followed by massage and passive motion. At the end of

FIG. 46.



eight weeks the patient was discharged, with an excellent result. Seen one year later the patient stated that he had absolutely no pain except after great exertion, especially standing. One finds that both legs are straight ; there is slight outward rotation and 2 cm. shortening. Inward rotation and abduction are restricted. Here we have the deformity of traumatic coxa vara, but with practically perfect function. Fig. 47 is an X-ray photograph of the case one year after injury. Although the deformity is still present, one sees at once that the union is better than in the cases observed in which there has been no treatment, and that the head rests in the acetabular cavity. Functionally the result

is perfect. I believe this case of Rammstedt's is the first one to be published in which we have an X-ray photograph four days after an injury and one showing the ultimate result one year later.

Case VI. This patient was seventeen years old. For three and a half years he has been doing unusually heavy work. Three months ago he received a direct trauma to the knee and over the hip. At that time he complained of a good deal of pain in the knee and limped a little, but continued to work. At the end of two days he experienced

FIG. 47.



pain in the hip, and at the end of the month the pain and limp had increased. At the end of two months he had to give up work on account of pain and go to bed. After staying in bed a week or so he noticed that the limp and the pain were less. After working again the pain and limp increased to such an extent that he could hardly bear his weight on the limb. He went to bed again for four days, followed by similar improvement; but on getting up again the pain returned, and he sought advice at the clinic. The examination showed the typical

deformity. The X-ray photograph (Fig. 48) demonstrates the fracture in the epiphyseal line, with a marked dislocation of the head downward and partly out of the acetabular cavity, while the neck of the femur rests against the anterior rim of the acetabulum. In this case the motion was very much restricted. The result of extension was a failure, so that operation was resorted to. The head and neck were resected and the trochanter placed in the acetabular cavity, with the leg in *abduction*. At the end of five months the patient was walking with a cane, without pain, the leg slightly abducted. He was able to flex the hip to a right angle. The position of the head in relation to the neck in this case is very similar to that of Sprengel's. Fig. 49 is a section of

FIG. 48.



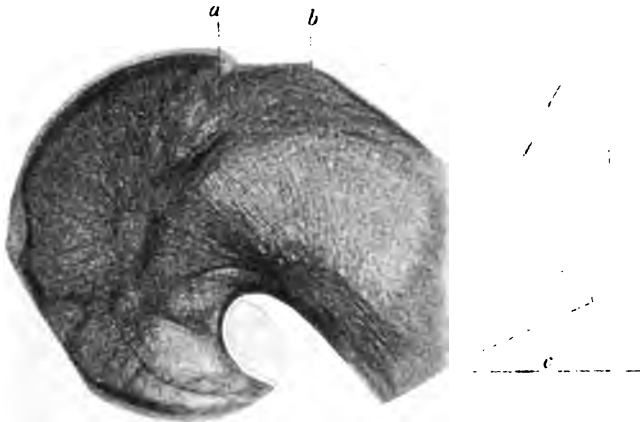
the specimen. It shows beautifully the line of fracture (*a*), in which microscopically every evidence of fracture was demonstrated. In this case the cartilage of the acetabular cavity and that covering the head were normal. The dislocation, however, was marked.

Case VII. was similar to Case VI. To me the most interesting is Case VI., in which following the injury there was very little loss of function, and the symptoms of *coxa vara stadica* slowly developed. The clinical picture is exactly that described by Hofmeister, and if one for a moment would lose sight of the trauma, not properly interpret the X-ray photograph, and put too much stress on the heavy work of the boy for two and a half years at the age of puberty, we would

consider it a typical case of coxa vara adolescentium of Hofmeister and Müller.

Case VIII. Patient was seventeen years of age. There was a history of rickets. One and a half years ago patient fell on his hip.

FIG. 49.



There was pain and he walked with a limp. He had no trouble except slight pain and slight limping for a year, when he began, at the age of sixteen years, to do very heavy work. Very gradually the pain in-

FIG. 50.



creased, and he noticed after a time that this leg became fatigued, and that there was restricted motion at the hip. After a short period of rest in bed there was improvement. Following work the symptoms returned,

so he sought advice at the clinic. The history in Case VIII. is very similar to that in Cases VI. and VII., except that the development of the symptoms were much more gradual and of longer duration, and had a distinct relation with the beginning of heavy work. The examination showed the typical deformity. The X-ray photograph, similar to the others here reproduced, showed a fracture between the head and neck. The operation was after Kocher's method, in which the head, neck, and trochanter were resected; the upper end of the shaft was placed in the acetabular cavity, the leg in the abducted position. It was noted at the operation that the acetabular cavity was widened; the upper rim was thickened and covered with a new bony growth. I have observed this in healed tuberculosis of the hip.<sup>1</sup> The head was almost entirely out of the acetabular cavity. Fig. 50 is a section of the specimen. In all of these eight cases the typical deformity was present—shortening, adduction, outward rotation; the trochanter was not only elevated, but prominent. In addition in every case 2 or 3 cm. below the anterior iliac spine one felt a hard prominence, which was due to the fractured neck projecting anteriorly. In one case only (Case IV., seen four days after the injury) there was *abduction*.

**Differential Diagnosis in Conditions about the Hip-joint and Upper End of the Femur.** The observations of Rammstedt, Whitman, Joachimsthal, Sprengel, Kocher and others are of the greatest importance. Here we have positive observations demonstrating that after very slight injury to the hip in a child or young adult there may be little or practically no symptoms for some weeks or months, but gradually the separation at the epiphysis gives, the fragments dislocate, and we have the characteristic deformity and symptoms of a coxa vara. If untreated for some time the dislocation may be so great and the restriction of motion so marked that there is no possible relief except from operation; excision of at least the head or the head and neck of the bone. It seems unnecessary to follow Kocher's plan of complete excision of the upper end of the femur. The results of these operations, although not as good as the results in cases seen earlier and followed by proper treatment, are very satisfactory. The pain is relieved, the leg is strong, and there is some motion at the hip-joint. There will always be shortening, but the shortening will be much less if only the head is excised or the head and neck and the remainder of the shaft placed in the acetabular cavity. Therefore, when one sees a patient a few days or weeks after the injury to the hip, the possibility of a fracture at the epiphysis or even at the neck must be borne in mind. Frequently the most careful measurement will demonstrate no shortening. One should

<sup>1</sup> Johns Hopkins Hospital Bulletin, January, 1900.



never allow such a patient to walk without the X-ray photograph positively excludes a fracture.

Alsberg<sup>1</sup> contributes a second article on the theory and differential diagnosis of coxa vara. His first article was carefully reviewed in *PROGRESSIVE MEDICINE* for December, 1899. In this second article Alsberg adds nothing particularly new, and it is chiefly concerned with a more or less theoretical discussion with regard to his methods of measurement of its angles of curvature of the neck, and the etiological relations of coxa vara and coxa valga, genu valgum and varus, and different forms of club-foot. Especially is the discussion concerned with that splendid monograph by Albert,<sup>2</sup> of Vienna.

Bähr,<sup>3</sup> of Hanover, contributes an article on the teaching of coxa vara. Bähr is chiefly concerned in the discussion of Sudeck's<sup>4</sup> article, and claims that the crest regarded by Sudeck as a strengthening ledge of the tension arch simply represents a roughness at the insertion of the joint capsule. However, I think that Bähr leaves the question still unsettled, and Sudeck's anatomical observations should be considered one of the best contributions to the anatomical study of curvature of the neck of the femur.

**TREATMENT OF CURVATURE OR FRACTURE OF THE NECK OF THE FEMUR.** This has been thoroughly discussed in *PROGRESSIVE MEDICINE* for December, 1899, and there is nothing new to add. Further experience has demonstrated the great importance of fixing the hip in recent cases for at least two months; in older cases for a longer period. Whitman<sup>5</sup> demonstrated a case before the New York Surgical Society. The patient was a boy, aged fifteen years, who four weeks previously was injured while playing foot-ball. Clinically the X-ray demonstrated a separation of the epiphysis. Whitman's treatment was with a very convenient form of walking apparatus, which had been used at the Hospital for Ruptured and Crippled in all cases of epiphyseal separation or fracture of the neck of the femur in early life. It consists essentially of a plaster-of-Paris spica bandage reaching to the knee, including the hip and pelvis, supplemented by a traction hip splint. By this means the weight of the body is removed and sufficient traction is exerted to overcome the muscular spasm. Whitman advises that this appliance should be worn for a number of weeks.

In the absence of the X-ray, or even in doubt from the X-ray photo-

<sup>1</sup> *Zeit. f. Orthopädische Chir.*, 1899, Bd. vii., Heft 2 and 3. p. 364.

<sup>2</sup> *Zur Lehre von der sogenannten Coxa vara und Coxa valga.* Alfred Hoelder. Wien., 1899. This reference was incorrectly given through a typographical error in *PROGRESSIVE MEDICINE* for December, 1899.

<sup>3</sup> *Arch. f. klin. Chir.*, 1900, Bd. lxi., Heft 2, p. 533.

<sup>4</sup> Discussed in *PROGRESSIVE MEDICINE* for December, 1899.

<sup>5</sup> *Annals of Surgery*, February, 1900, vol. xxxi., p. 258.

graph, the patient should be treated for fracture, extension in bed at least two or three weeks, followed by fixation in plaster or some hip splint for two or three weeks longer. Even with the history of trauma, which is followed gradually by pain, limp, and deformity, the possibility of tuberculosis of the hip or chronic osteomyelitis of the upper end of the femur must be borne in mind. In the first observations, agreeing with Hofmeister, Sprengel did not think that the X-ray photograph would make a positive differential diagnosis, but the recent observations of Joachimstahl, Kermisson, Whitman, and Rammstedt show that in the majority of cases the line of fracture is clearly depicted in the X-ray photograph. The treatment, however, for the curvature of the neck of the femur, whether it is due to fracture or bending from other causes, is the same. An attempt to exclude tuberculosis must be made by the tuberculin test, and if there is any possibility of tubercular or pyogenic infection there is absolutely no contraindication to the exploration of the hip-joint and the upper end of the femur through the anterior incision, recommended by Barker.<sup>1</sup>

**TREATMENT OF FRACTURE OF THE NECK OF THE FEMUR IN ADULTS.** The observations of Scudder<sup>2</sup> on sixteen cases of fracture of the neck of the femur, treated in the Massachusetts General Hospital by gentle traction and immobilization for periods varying from a few weeks to a few months, followed by the use of crutches for a number of weeks, is very suggestive. Scudder states that nearly all the cases were unimpacted, either primarily or secondarily. At the time of the accident seven cases were between forty-two and forty-seven years; the remainder over fifty years; three were over sixty years. These cases have been examined from two and a half to twenty-four and a half years after the accident. Thirteen of the sixteen had impairment of the functional usefulness of the leg. There is a weakness of the limb in many of the cases, and the crutch is used. All movements of the hip-joint are somewhat restricted; there is decided atrophy of the muscles of the thigh, buttocks, and calf of the leg; there is a decided limp, which if not requiring a crutch does require a cane. There is pain in the hip, extending down the thigh, even to the sole of the foot; pain at night, pain on going up stairs and in stooping over. In only two out of sixteen cases could it be said that the leg was functionally useful. Scudder does not state whether there was non-union in any of the cases. In practically all of these sixteen cases, treated no doubt by the best method of extension and immobilization, we have as the ultimate result the deformity and the painful symptoms of a coxa vara

<sup>1</sup> See Early Exploratory Operations in Tuberculosis of the Hip. Bloodgood. Johns Hopkins Hospital Bulletin, January, 1900.

<sup>2</sup> Loc. cit., p. 252.

*statica*. I have recently examined practically all the patients treated in Professor Halsted's clinic in the Johns Hopkins Hospital during the last ten years. Our results, I think, are more satisfactory than those reported by Scudder. There are a number of cases with good functional results—that is, the patients are able to walk without a cane or crutch, and do not suffer from pain; in every one of these cases, however, there is some shortening. In many of the cases the deformity is more marked—shortening and outward rotation, and in some cases adduction with restriction of motion. A few of these cases have a functionally good result, but the majority have to use a crutch or cane, and suffer some pain. In a few cases there has been non-union. In these cases there is absolutely no result, although there is very little restriction of motion in the hip-joint. When the patient walks the trochanter rises every time the weight is thrown upon that limb; the patient cannot walk without crutches, and even with crutches there is pain. These observations would seem to indicate that there is much room for improvement in the treatment of fracture of the neck of the femur in adults. It would appear that, after the usual treatment with extension and fixation in bed, to allow the patient to walk, bearing the full weight on the hip without any support, is followed after a certain length of time by (perhaps) increase of the deformity, and, with this, increase of the disability and discomfort. Future observations may demonstrate that these cases should wear some form of the hip splint or support for a number of months, perhaps a year, after the injury, to prevent further bending of the neck of the femur.

In order to insure a more perfect approximation of the fragments, more rapid and solid union, Nicolaysen<sup>1</sup> has recommended nailing for recent fracture. He states that in the hospital in Christiania since 1894 he has practised this method. His observations so far cover twenty-one cases, eight male and thirteen female. After the reduction of the fracture a steel triangular nail, about 12 cm. in length, is driven into the trochanter, and so through the neck into the head, fixing the fragments. The limb is then immobilized in plaster, which remains in place from ten to twelve weeks. The nail is removed at the end of the second or third week through a window cut in the plaster. The results have been excellent. The actual shortening has averaged 4 cm. He states that there has been no adduction. The nailing can be done, as a rule, without narcosis; many of his patients were old and decrepid. I am sorry to be unable to get the original article,<sup>2</sup> in order to discuss this paper more in detail.

<sup>1</sup> *Centralbl. f. Chir.*, 1900, Bd. xxvii., p. 598.

<sup>2</sup> *Fracture of the Femoral Neck Treated with Nailing*. *Nord. med. Arkiv*. N. F., Bd. x., No. 29.

*Excision of the Head of the Femur in Old Fractures of the Femoral Neck.* For at least two years I have felt that excision of the head of the femur in cases of ununited fracture of the neck would be a justifiable procedure, and the result would give a limb solid at the hip-joint and with good function. The operations for cases of coxa vara by Sprengel, Kocher and others have clearly demonstrated this; so that in cases of non-union the head and part of the neck should be removed and the remainder placed in the acetabular cavity. In addition, in cases of fracture of the neck of the femur in which union has taken place, but with such marked dislocation that there is great deformity of the leg associated with pain and discomfort, in these cases unquestionably the operative treatment would give a limb on which the patient could walk, with practically no discomfort and with little deformity except shortening and perhaps more or less fixation of the hip-joint. Recently, Reese<sup>1</sup> has reported on this subject. His patient was a woman, aged fifty-nine years, observed March 9, 1899. Following the usual treatment, non-union resulted, and in addition to the non-union there were severe pains. The diagnosis was confirmed by the skiagraph. At the operation not only the head but the end of the trochanter was resected. Reese states he was unable to remove the head without doing this. In four weeks the patient was allowed to walk, with the hip fixed in a Bruns splint. In six weeks there was complication of thrombosis at the femoral vein. Ultimate result, however, was excellent. The patient was able to walk without a cane and to stand alone on the affected leg. There was shortening of 3 cm. and some restriction of motion. The X-ray photograph demonstrates that the lower part of the neck rests against the upper rim of the acetabulum, while the trochanter minor is in the acetabular cavity. Marten<sup>2</sup> reports two further cases which were operated on in the Charity Clinic in Berlin; one patient, aged thirty-nine years, was treated four months after the accident; the other patient, aged fifty-eight years, was treated two years after the accident. In both cases there were good results. All these observations would suggest that it would be a good plan to resort to operation in all our cases of fracture of the neck in which there is either non-union or little, if any, functional use of the limb.

## SURGERY OF THE JOINTS AND BONES.

The pathology, diagnosis, and treatment of diseases of the joints and bones have such a close connection that they should be considered together. The majority of pathological changes in the joint soon lead

<sup>1</sup> Centralbl. f. Chir., Bd. xxvii., p. 143.

<sup>2</sup> Ibid., p. 146.

to the involvement of the bone or its periosteum, the reverse being true of primary conditions in the bone. The most recent and at the same time the best and most complete publication on diseases of the bones and joints will be found in the *Deutsche Chirurgie*,<sup>1</sup> 1899.

In this publication Prof. Karl Schuchardt, of Stettin, considers the diseases of bones and joints exclusive of tuberculosis, while Prof. Fedor Krause, of Altona, considers tuberculosis of bones and joints. In the following discussion of the recent literature these two authors will be quoted extensively, not only because of their excellent original observations, but also for their complete consideration of the most recent literature.

In no other diseases is a knowledge of the pathology and bacteriology of greater importance as an aid to early differential diagnosis and treatment than of the bones and joints. Surgeons and physicians in this country must fully recognize the importance of this knowledge, which should be acquired in properly equipped laboratories.

Perhaps in no other diseases (especially of the joints) are the two great specialties, medicine and surgery, brought more into contact in the consideration of the clinical differential diagnosis, and in recent years the most important knowledge has been derived through bacteriological, pathological, and chemical investigation, and also by the work of the neurologists, on the relation between diseases of the nervous system to certain pathological changes in the bones and joints. Early diagnosis and treatment in the pyogenic infections of the bones and joints is one that should be impressed on the entire profession; delay increases tremendously the rate of mortality or leads to pathetic local deformities. Recent experience unquestionably demonstrates that early diagnosis, followed by proper operative interference, not only saves life, with few exceptions, but saves the limb, with very little, if any, deformity or limitation of function. In spite of this fact, it is still true that the majority of cases of not only acute pyogenic infections of the bones and joints, but also of tuberculosis, are admitted to the large clinics and hospitals throughout the world in the late stages of the disease, fearfully emaciated from prolonged septic infection and with local pathological changes which make it impossible in the majority of instances to restore the limb with complete function. In looking over some four hundred cases of osteomyelitis in the clinic of the Johns Hopkins Hospital during the past eleven years, barely 5 per cent. have been admitted in the early stage of the disease; the others, weeks, months, and years later. The knowledge necessary for the ability to make a differential diagnosis at this early period is open to everyone, and there are not

<sup>1</sup> *Deutsche Chirurgie*, Billroth and Luecke, Parts 28 and 28a, Stuttgart, 1899.

many sections in this country where one will not find surgeons ready to institute the proper surgical intervention when the patients are referred to them for treatment.

**Traumatic Arthritis.** Given a patient with an indirect or direct trauma to a joint, one must exclude at once the possibility of a fracture or dislocation. Following a contusion or distortion of a joint there are certain immediate and remote pathological changes. These changes, with their clinical manifestations, must be thoroughly understood before one can institute proper treatment.

*The immediate pathological changes in traumatic arthritis may be a more or less stretching and tearing of the different ligaments about the joint and a varying amount of hemorrhage and inflammatory exudate, both into the joint cavity itself and into the extrasynovial tissues. Some possible injury to the articular cartilage must also be borne in mind. The location and extent of stretching or tearing of the tissues about the joint or injury to the cartilage are in the majority of cases very difficult to clearly make out, yet such a possibility should always be borne in mind in the after-treatment. The intracapsular exudate, designated as effusion, and the extracapsular exudate, clinically called œdema, are easily distinguished.*

**PYOGENIC INFECTIONS IN ACUTE TRAUMATIC ARTHRITIS.** In the first hours and few days of traumatic arthritis the possibility of a pyogenic infection should always be borne in mind. Such an infection is rare, but always possible, on account of the lower local resistance of the injured tissues. Clinically, this should be recognized by the general signs of fever and leucocytosis and the increased local signs; however, in non-infected traumatic arthritis there may be fever. So far there are but few observations on the leucocyte count. In some contusions with excessive hemorrhagic and inflammatory exudate there may be intense local symptoms. For this reason in a few cases it will be difficult from the general and local symptoms to make a sufficiently early diagnosis without the aid of a bacteriological examination by cover-slip and culture of the joint effusion. Aspiration of the joint in traumatic arthritis is distinctly indicated, and should be done early. It is, without doubt, the best treatment for the effusion, because it relieves the tissues at once of a certain amount of pressure and prevents the over-distention of the capsule of the joint, which when not relieved is the frequent cause which leads either to a chronic condition of hydrops or a tendency to recurrent hydrops following slight trauma. Demonstrating the aspirated fluid to be sterile excludes the necessity of further operative interference. The presence of bacteria at the first or later aspiration indicates an immediate arthrotomy and irrigation. In *PROGRESSIVE MEDICINE* for December, 1899, page 233, I reported

two cases which illustrated the importance and aid of aspiration and its bacteriological study. Both were cases of traumatic arthritis of the knee, with effusion following a contusion. One was admitted two days and one three days after the injury. In both the local signs were equally intense; both had fever ( $103^{\circ}$  to  $104^{\circ}$  F.); in one the aspirated effusion contained leucocytes, but no bacteria. Following the aspiration the local and general symptoms disappeared within twelve hours. In the second case the aspirated fluid, which was not more cloudy than the first, and contained no more leucocytes, showed numerous streptococci on the cover-slips and an abundant growth of streptococci in the culture within twenty-four hours. No relief followed the aspiration, and the effusion reaccumulated. After delay of about eighteen hours the joint was opened and irrigated. Recovery followed, with perfect function.

Unquestionably the pyogenic infection in traumatic arthritis with effusion is rare. I have observed it three times in about sixty cases of traumatic arthritis of the knee-joint. In one of these it was associated with osteomyelitis of the lower end of the femur. This brings up the second important fact to be remembered: that following contusion of a joint the pyogenic cocci may attack the medullary tissue of one of the neighboring bones. In such an instance the probabilities are that the joint effusion would also be infected. When arthrotomy and irrigation are not followed by immediate relief the possibility of infected osteomyelitis should be borne in mind and the bone medulla at once explored. The observation of my own, just mentioned, the local and general symptoms were but slightly relieved by the arthrotomy and irrigation (the aspirated joint effusion contained the staphylococcus pyogenes aureus). However, improperly thinking that the fever and local symptoms were still due to the joint infection, a second operation was delayed a few days, at which time the general condition was so bad and the destruction of the bone was so advanced that amputation was necessary. One experience like this should be sufficient. If the aspirated fluid is sterile, but the local and general symptoms continue, one should not delay long in exploring the bone. I believe that future leucocyte blood-counts will help us in differential diagnosis. I doubt if there will be no leucocytosis, especially an increasing one, without pyogenic infection of the bone or joint.

**PATHOLOGY OF ACUTE TRAUMATIC ARTHRITIS.** I believe the term arthritis is a better one than synovitis, and, as Schuchardt writes, it may be confined either chiefly to the superficial layer of the synovial membrane, in which case there is always a marked effusion, or the exudate may be chiefly in the deeper tissues, or both may be combined. The involvement of cartilage and bone is simply an extension of the inflam-

mation from the soft parts of the joint. This takes place seldom, if ever, in simple acute traumatic arthritis without pyogenic infection. The appearance of a joint after contusion is well described by Billroth.<sup>1</sup> We find a varying degree of hemorrhage into the joint cavity and into the tissues; the usually pale synovial surface is ecchymotic. There is an exudate of fibrin and serum both into the joint cavity and into the tissues. We seldom observe such a joint unless the patient dies from other injuries.

**TREATMENT OF ACUTE TRAUMATIC ARTHRITIS.** *Contusion or Distortion of a Joint.* Having excluded the possibility of a fracture or dislocation, we have to bear in mind the immediate treatment of the exudate and the possible lacerations of tendons or cartilage. The exudate is best treated by aspiration of the joint if the effusion is excessive (as has already been discussed, this is also important for the bacteriological study).

The application of heat and massage, followed by rest, with tight bandaging, are the best means to aid the circulation in reabsorbing the exudate. Properly treated, the contused joint should have its application of hot-water or air, followed by massage, at least once or twice a day. In the interval the joint should be firmly bandaged and kept at rest. If one could be positive that the only pathological lesion was the exudation, passive motion should be added to the massage, and the supporting bandage should be removed in a few days and the patient urged to use the limb. In milder cases this can always be done; the supporting bandage, however, might be retained a few days or a week longer after the patient has begun using the limb. In more severe cases, or in the milder cases in which pain and the loss of function persist, the possibility of a lacerated or stretched tendon or an injury of the cartilage must be borne in mind. Such an injury takes longer to heal, and during the healing the joint should be supported by a properly applied bandage or some form of a simple apparatus. If one does not support such a joint there is a risk that the relaxation of the tendons will become a permanent one and the joint not only painful, but distinctly weak. The absolute rest which would be good for the relaxed and torn tendon is, however, always bad for the contused joint. Prolonged fixation is frequently followed by permanent cellular changes, both in the synovial membrane and the surrounding joint tissues, which restrict motion and in some cases lead to permanent ankylosis.

Permanent rest in any fixed bandage all authorities condemn, and yet it is frequently the practice to place a contused joint in plaster

<sup>1</sup> General Surgical Pathology and Therapeutics, fourth edition, 1890.



for weeks and often months. From the very first there should be massage. A few days later passive motion, increased in degree from day to day. In the interval a bandage. If the continuation of pain and the relaxation of the joint indicate a laceration or stretching of the ligaments, some form of support should be applied until the healing and strength of the tissues are restored ; but during this time there should be daily massage and passive motion. This is the most important point to be impressed upon the general practitioner. Patients should be compelled to walk on the injured joint, if properly supported, regardless of pain. Massage and passive motion should be instituted and continued regardless of pain. This pain and tenderness will, however, soon disappear. If a joint unsupported is painful when used, but painless when properly supported, this is an indication of a laceration or stretching of the supporting ligaments, and the support should be continued even for months until this disappears.

Hoffmann,<sup>1</sup> of St. Louis, in an article entitled "A Treatment for Acute Serous Synovitis Permitting of Joint Function," advocates a special method of fixation with adhesive plaster, very similar to that advocated by Gibney,<sup>2</sup> of New York, in 1893. The case reported gives the method in detail. The patient was a carpenter, aged thirty-seven years, suffering with contusion of the knee, which was rapidly followed by effusion into the joint. The treatment began forty-eight hours after the accident. A pad of cotton was placed in the popliteal space and the parts were covered with a close-fitting stocking leg. Over this adhesive plaster was applied in the following manner : A strip of about an inch wide and thirty inches long was made to encircle the leg, beginning six inches below the patella. At a point where the conical shape of the calf caused the strip to alter its course a second strip was applied, overlapping the first. This was repeated until the limb to a point six inches above the patella was completely encircled. A muslin bandage was placed over the adhesive strips. The dressings were changed at the end of twenty-four hours, because, on account of the resorption of the effusion, they had become loose. They were changed when the occasion indicated it up to the twenty-second day, when the patient was discharged, cured. Hoffmann states that he has treated with this adhesive plaster method 156 cases of synovitis, with most gratifying results. He also says that, in place of a stocking under-dressing, one may use glazed sheet-cotton, and in some cases he applies the adhesive plaster directly on the skin, especially in those cases where the swelling is slight or later on in the treatment when it has consider-

<sup>1</sup> New York Medical Journal, January 27, 1900. vol. lxxi., p. 125.

<sup>2</sup> New York Polyclinic, January, 1893.

ably subsided. He states, however, that frequently the skin becomes sore and compels one to resort to a protective under-dressing. He states that, as a rule, he permits his patients to use the limb in any way that does not cause pain or discomfort. On four occasions Hoffmann, after aspirating the knee, applied this adhesive plaster dressing and allowed the patients to walk, with good results. Personally, I believe that the effusion should be aspirated at once if it can be done with the proper precautions. There are serious objections to applying adhesive plaster directly to the skin; not only does it irritate the skin and force one later to use an under-dressing, but it does not allow the necessary frequent removal for passive motion and massage. The tight-fitting stocking leg advocated by Hoffmann impresses one as an important adjunct. Over this a crinoline bandage or adhesive strip may be applied. Later, if there is no serious injury to the joint's ligaments, a firmly and properly applied flannel bandage will be sufficient.

Hasebroek,<sup>1</sup> in his excellent article on the "After-treatment of Sprains of the Hand-joint, Knee-joint, and Foot-joint," emphasizes the points just discussed and advocates the use of a supporting apparatus in those cases in which the symptoms indicate that a more serious injury is present in the affected joint. His observations unquestionably prove that we must differentiate and recognize those cases of joint injuries which need this more or less prolonged use of a supporting apparatus. The

properly applied bandage is sufficient for the early days, or possibly a couple of weeks, but is by no means the best or the ideal method for a longer support. His apparatus is easily removed, so that passive motion and massage can be performed daily. It allows flexion and extension of the joint within limitations, and supports the joints chiefly laterally. One cannot but be impressed by his cases and the results and by the simplicity of his apparatus. A plaster cast is made of the joint; from this a mould over which the leather support is fitted. Fig. 51 shows the apparatus as applied to the wrist, Fig. 52 that applied to the knee, and Fig. 53 that applied to the ankle. These three joints are unquestionably the most common which

require such treatment, and unquestionably in this country the after-treatment of these cases is either neglected or badly done. The plaster

FIG. 51.



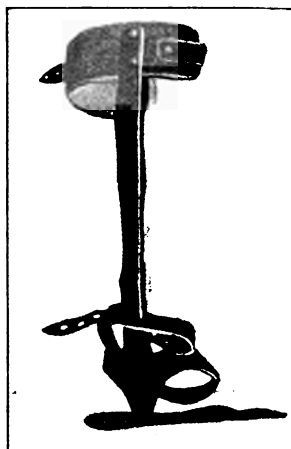
<sup>1</sup> Münch. med. Wochenschr., July 25, 1899, vol. xvi., p. 983.

or crinoline bandage is not proper for prolonged fixation. The method recommended by Gibney and also by Hoffa in his text-book, which consists of incasing of the ankle-joint with implicated strips of adhesive plaster, is an excellent and well-known one, and serves its purpose for a short time, but it does not allow the daily massage and passive motion, which should not be neglected.

FIG. 52.



FIG. 53.



**The Remote Effects of Contusion or Distortion of Joints.** One must always bear in mind the possibility of a detached piece of articular cartilage which may later on manifest itself, first by recurrent attacks of arthritis with effusion, and later by the movable body itself, the formation of joint lipoma, also the dislocation of the semilunar cartilage of the knee-joint, which may not have been recognized at the time of the first injury. (These have been discussed in *PROGRESSIVE MEDICINE* for December, 1899.) The persistence of the local symptoms or the recurrence of the same may be due to the localization of a tubercular or pyogenic infection, or the onset of new growth, or to a metastasis from a hitherto unrecognized primary growth in some other part of the body, as the prostate or thyroid. The joint symptoms may persist or relapse, due to a chronic or acute gonorrhoeal infection, or may be the only joint manifestation of a rheumatic or gouty individual.

**The Immediate or Later Study of a Simple Contused Joint** is filled with many possibilities for differential diagnosis. Good results

depend entirely on the early recognition and proper treatment of the exact cause.

Schulze and Berge<sup>1</sup> draw attention to the relation between joint rheumatism and trauma. This relationship is a difficult one to demonstrate, but clinically it is frequently observed, and must be borne in mind.

**Acute Arthritis or Synovitis.** The intensity and duration of the local symptoms about the affected joint are the factors that classify the condition as an acute one. There may or may not be general symptoms. One or more joints may be affected, in which instance we speak of monarticular or polyarticular arthritis. The causes of acute arthritis are numerous. I feel that the most important classification which should be made at once is the division into two groups: (1) Those in which the joint effusion or periarticular cedema is sterile, and (2) those in which bacteria are present. We might speak of these two groups as non-infected and infected acute arthritis, meaning by the word infected the actual presence of some pyogenic cocci in the joint effusion or periarticular exudate. This classification is important because the immediate treatment depends on the presence or absence of pyogenic cocci. This has already been discussed in acute traumatic arthritis following contusion or distortion, in which pyogenic infection is rare, but always possible, and must be constantly borne in mind.

**Wounds of the Joint.** In any form of penetrating wounds which open the capsule of the joint the possibility of pyogenic infection is greatly increased. Seen early, within twenty-four to forty-eight hours, it is unquestionably the better plan to disinfect the external wound, to disinfect the skin about it, and then, under proper precautions, to enlarge the wound, open the joint, and irrigate it. Drainage would depend upon the bacteriological examination of the fluid in the joint and the extent of the contusion and laceration about the original wound. In the presence of bacteria in the joint effusion it would be safer not to suture the capsule, but to leave it open for later joint irrigations if the symptoms required it. If the effusion was sterile the capsule of the joint should be closed by suture. If the external wound can be easily completely cleaned and the torn tissues excised, so that the remaining tissues have good circulation, and there is no bacteriological infection, this wound can be closed with a small protective drain. In the presence of any degree of infection or any extent of lacerated and contused tissue the external wound should be left open to heal by granulation. Therefore, in a recent wound communicating with the joint one should not wait for symptoms of infection, but at once, after proper disinfection, follow the

<sup>1</sup> *Monatsschrift f. Unfallheilkunde*, 1899, No. 12, and *Centralblatt f. Chirurgie*, Bd. xxvii., No. 6, p. 172.

treatment just advocated. This is also true of bullet wounds of the joints.

Exceptions to this rule should be made on the field of battle or in any locality where the surgeon would be unable to perform the operation under proper precautions, because in bullet and other penetrating wounds of the joint there is always a possibility that either there has been no infection or that the tissues can take care of the few bacteria, and the wound will heal without any pyogenic arthritis. All military authorities seem to agree on this conservative treatment and wait for the symptoms of infected acute arthritis before resorting to arthrotomy, irrigation, and drainage. However, I believe that in civil practice, where the operation can be performed under proper precautions, the treatment first advocated will give the better results.

When a penetrating wound of the joint is seen later than forty-eight hours after the injury the treatment depends upon the bacteriological examination of the fluid and the local and general signs of pyogenic infection. After forty-eight hours the primary wound should have healed, and if there had been infection there would probably be some local and general symptoms. These, however, might be due to the injury and not to infection, as already described under contusion of the joint. In such a case, if there are no local symptoms and no effusion, there is no indication for treatment except rest and the dressing of the external wound. If there is still an effusion it should be aspirated. If it is sterile, aspiration should be sufficient. If pyogenic cocci are present in the effusion arthrotomy and irrigation should be performed at once.

**Acute Arthritis or Synovitis not Associated with Injury.** This form of arthritis, with its many causes, is a difficult one in which to make a differential diagnosis, and the proper treatment is not yet on a scientific basis.

**Pathology of Acute Exudated Arthritis or Synovitis.** Schuchardt<sup>1</sup> gives the following classification, which is made dependent upon the character of joint effusion and extracapsular exudate. This exudate may take place in the acute, subacute, or chronic forms of arthritis. We must first distinguish two primary groups: one in which inflammation is confined chiefly to the inner layer of the synovial membrane, and which is characterized by a marked effusion into the joint. This effusion may be: (1) Serous, (2) sero-fibrinous, (3) fibrinous, (4) hemorrhagic, (5) purulent. Schuchardt does not go into the bacteriology of this exudate, which, however, is a very important factor. Numerous observations in the literature and of my own have demonstrated that some form of pyogenic cocci may be associated with

<sup>1</sup> Loc. cit.

any of the five different exudates. In the early hours or days of the pyogenic exudate the effusion is serous or sero-fibrinous. If not relieved it quickly becomes purulent. It is seldom, if ever, distinctly hemorrhagic, although it may contain a number of red blood-corpuscles. The pure hemorrhagic form is usually associated with traumatism or the hemorrhagic diseases, such as scurvy, hæmophilia, and purpura. The exudate is seldom purulent without the presence of pyogenic cocci. However, every now and then one finds a sterile, purulent exudate, for example, as after traumatism, in gouty, rheumatic, or gonorrhœal arthritis, in the irritative arthritis so frequently associated with acute or chronic pyogenic osteomyelitis or tubercular osteomyelitis; rarely in Charcot's joints or other forms of arthropathies dependent upon lesions in the nervous system. Not uncommonly in multiple pyæmic arthritis the effusion may be purulent and sterile, yet in the majority of instances in those cases which have been carefully studied bacteriologically a sterile joint effusion is either serous or sero-fibrinous, and microscopically one finds but few leucocytes. In Schuchardt's second group the inflammation is confined chiefly to the subsynovial tissue, and is characterized by marked periarticular œdema. Both conditions, effusion and periarticular exudate, may be associated.

**Changes and Destruction in the Bones, Cartilage, Tendons, Bursa, and Muscles about the Joint** are simply an extension from the inflammation of the synovial membrane or due to the direct action of the synovial exudate on the cartilage.

**Primary and Secondary Arthritis.** In every case of single or multiple joint inflammation the clinician must at once attempt to ascertain whether the synovitis is a primary one or secondary to some inflammatory focus in the neighboring bone. In the latter instance not only the arthritis, but its cause, the osteomyelitis, must be treated to insure a favorable result.

**Treatment of Acute Arthritis in which the Effusion or Exudate is Sterile.** Having demonstrated by aspiration the sterility of the exudate, no matter what its primary cause, the treatment of the arthritis is a conservative one—rest and fixation in the early days, associated with careful massage and passive motion and the application of external heat or cold. The primary cause must be sought for and treated. This will be discussed later under Gout, Rheumatism, etc.

**Treatment of Acute Arthritis in which the Effusion or Exudate Contains Bacteria.** Any form of single or multiple arthritis in which observations have demonstrated that the exudate is, as a rule, sterile, may become secondarily infected with any of the pyogenic cocci, which, however, are secondary invaders and not the primary cause of the arthritis. The most common causes of pyogenic arthritis are (1) pene-

trating wounds of the joint; (2) extensions through the lymphatics to the joint from the infected wound to the extremity; (3) metastatic infection from a primary focus in any part of the body (pyæmia); (4) direct extension from a focus of pyogenic osteomyelitis.

The most important are the infected arthritides associated with pyogenic osteomyelitis. This subject has been fully discussed in *PROGRESSIVE MEDICINE* for December, 1899, under Osteomyelitis. Especially in young children the joint symptoms mask the bone inflammation, and it is the most common error, even among experienced surgeons, to open and irrigate the infected joint without exploration of the bone. When one finds in the joint effusion the streptococcus, the pneumococcus, the staphylococcus aureus or albus, and the arthritis is not associated with a penetrating wound or infections of the soft parts near the affected joint, the probabilities are that the arthritis is secondary to a bone infection.

Demonstrating the presence of pyogenic cocci in the joint effusion, arthrotomy and irrigation of the joint should at once be performed and, in the instances just discussed, the neighboring bone explored.

König,<sup>1</sup> in the paper entitled "Evolutions in Surgical Technique of Operations on Joints," read before the German Surgical Congress in April, 1900, writes as follows: "While fully recognizing the merits of puncture, with disinfecting irrigation, it is evident that the typical joint drainage which was at first welcomed with such enthusiasm, and in many cases actually sufficient, has, however, not fulfilled everything." Thus, for instance, grave streptococci and staphylococci infections are often resistant against it, and only larger incisions which expose the joint sacs to their widest extent lead to a happy result. At the knee one makes two lateral incisions and eventually popliteal and calf incisions. All perforations from the joint sac tend to gravitate in the interstitia of the muscles at the upper thigh anteriorly and in the lower thigh between the posterior calf muscles; these infiltrations must be exposed by long incisions. In a form of gonococcus infection in which there is a little joint effusion, but marked periarticular infiltration which has a tendency for grave contractures and ankyloses of the joint, one must not only open the joint by lateral incisions, but make numerous incisions in the infiltrated periarticular tissue. In a very grave suppurating knee-joint König advises to connect the two lateral incisions by a transverse incision below the patella, thus completely opening the joint. In the discussion Franke remarked that he had taken the same position for years, and strongly recommended numerous incisions into and about the joint, with iodoform-gauze tamponing of

<sup>1</sup> *Centralblatt f. Chirurgie*, 1900, Bd. xxvii., No. 28, p. 27.

the pus cavity. Schede, of Bonn, opposed König's advice, and stated that from his experience most of these joints, provided the capsule is intact, will heal by simple antiseptic irrigation. König did not dispute this, and explained that his more extensive treatment was to be confined to those grave cases of joint infection which heretofore seemed to demand amputation.

In this discussion very little was said about bacteriological investigation and the relation between (1) the duration of the infection and (2) specific pyogenic organisms. Recent experience of my own and the authorities quoted in *PROGRESSIVE MEDICINE* for December, 1899, seem to justify the following conclusions: Given an infected joint of a short duration—say, twenty-four to forty-eight hours—one should aspirate the effusion. If the specific micro-organism is the typhoid bacillus, the gonococcus, the pneumococcus, or the streptococcus, and the effusion is not very purulent, one might wait twenty-four hours for the result of this treatment. In the few cases in the literature aspiration of the effusion infected by the typhoid bacillus has been followed by good results. This is also true now and then with the gonococcus, more rarely with the pneumococcus, and still more rarely with the streptococcus. An effusion infected with the staphylococcus aureus or albus should be followed by arthrotomy and irrigation at once. The safest rule, however, is to open and irrigate a joint the moment the presence of pyogenic cocci have been demonstrated in the effusion (with the single exception of the typhoid bacillus). Arthrotomy of any joint, even the hip, through the anterior incision, is a simple procedure. It can be performed under local anæsthesia. The earlier the synovial sac is relieved of its tension by incision and disinfected by irrigations the greater the probabilities are that the function of the joint will be restored. Delay is associated with cellular changes in the synovial and periarticular tissues, which, even when relieved at this later date, are followed by the formation of excessive scar tissue, which permanently restricts the function of the joint.

In those cases of grave joint infection in which the capsule is ruptured and periarticular infiltration and abscesses have taken place, König's advice of freer and more numerous incisions should be followed. In every case, as stated before, the possibility of a bone infection should be borne in mind.

### **GONORRHOEAL ARTHRITIS.**

In *PROGRESSIVE MEDICINE* for December, 1899, I wrote that it should be the rule in gonorrhoeal arthritis to aspirate the joint. When the effusion is purulent, and when the gonococcus is found in the cover-slip



or culture, arthrotomy should at once be performed and the joint irrigated with a solution of 1:1000 bichloride of mercury (to prevent absorption of the bichloride an Esmarch bandage should always be placed on the limb above the joint). In the majority of cases the wound can be closed; in very virulent cases the wound should be left open, but drainage is unnecessary. So far in my own experience we have never had to open the joint a second time; even in cases in which the wound was left open without drainage the healing of the wound has been rapid. When the effusion is sterile one should depend upon simple aspiration and non-operative measures (heat or cold). It is very important to note here that after the aspiration of the joint and demonstrating the sterility of the fluid the joint should be examined at least once in twenty-four hours. Should the effusion reaccumulate it should be aspirated again and studied at once for the gonococcus. The presence of a few gonococci in a slightly cloudy fluid in which one finds but a few leucocytes may be relieved by aspiration. If, however, at the end of twenty-four hours the fluid reaccumulates and is found to be more purulent, or if the clinical symptoms, pain and fever, are still present, arthrotomy and irrigation should not be delayed.

Such early operative interference indicated by bacteriological findings is not the usual practice in this country, and the usual authorities which reach the general practitioner do not help him much in the proper treatment of acute gonorrhoeal arthritis.

An arthrotomy and irrigation instituted early in a gonorrhoeal joint with a purulent effusion containing the gonococcus will be followed by a perfect result, with practically no impairment of the function of the joint, with hardly an exception; delayed, or not performed at all, restriction of motion or complete ankylosis is the rule. I have recently seen a patient in which the conservative treatment was followed. The knee-joint was ankylosed in a flexed position, and at the operation I found a bony ankylosis between the patella and the condyle of the femur. The upper synovial sac of the joint was completely obliterated and the synovial membrane replaced by scar tissue.

John O'Connor<sup>1</sup> writes from the British Hospital in Buenos Ayres as follows: "I have practised arthrotomy with irrigation and drainage in all cases of this malady, and so far my results tend to confirm the opinion stated in my first paper."<sup>2</sup> I cannot too strongly recommend surgeons to tackle this disease early." O'Connor then reports shortly ten cases, six of the knee-joint and one of the ankle-joint and wrist-joint each. In two cases two joints were involved, in one both knees,

<sup>1</sup> Lancet, London, December 9, 1899.

<sup>2</sup> Glasgow Medical Journal, December, 1897, and Annals of Surgery, February, 1898.

and in the other knee-joints and wrist-joints. Unfortunately, there are no bacteriological or pathological reports. The effusion is described as serous or slightly cloudy, with flakes of lymph in the majority of cases. In none of the cases is it described as being purulent. The results, however, in every case were excellent. It should, however, be distinctly borne in mind that it is unnecessary to open and irrigate a gonorrhœal joint unless the effusion contains the gonococcus; aspiration is sufficient; however, with good technique it does no harm to open and irrigate even a non-infected joint.

B. G. A. Moynihan,<sup>1</sup> of the Leeds General Infirmary, gives us a short and excellent clinical lecture of the joint affections of gonorrhœa. The classification adopted is that of Prof. König, of Berlin: (1) Hydrops (serous); (2) sero-fibrinous; (3) empyema (purulent); and (4) phlegmonous. It should be stated, however, that the first three forms are simply varieties of synovitis, with effusion, in which the inflammation is confined chiefly to the superficial layers of the synovial membrane, and is characterized chiefly by an effusion in the joints which may be serous, sero-fibrinous, fibrinous, hemorrhagic, or purulent. The phlegmonous form is that one in which the deeper layers of the synovial membrane are chiefly affected and clinically characterized by extra-articular œdema and not much effusion into the joint cavity itself. This latter classification is the best one to adopt for all forms of acute arthritis or synovitis, and is the one adopted and described by Schuchardt. This, of course, is a pathological classification, as Moynihan states. However, these pathological changes are common to all forms of acute arthritis, which differ only in the bacteriological findings which are the specific cause of the inflammation. Moynihan goes on to say that the hydrops variety is the least severe form, and usually attacks the knee. The arthritis is usually not severe. During the attack one joint becomes swollen from the effusion. The swelling is associated with very little pain or tenderness and no fever. The effusion generally disappears quickly, and recovery is but a matter of a few weeks. The function of the joint is never impaired. In the sero-fibrinous and the purulent forms the symptoms are more intense, both local and general, and more or less general ankylosis may follow. The phlegmonous form is the most serious. Effusion in the joint is absent or but slight. The extension of inflammation outside the joint cavity is marked and of a high grade. The local and general symptoms are extreme. The disorganization of the joint is rapid. Extra-articular abscesses may form, and ankylosis takes place rapidly.

Moynihan also speaks of the fact that gonorrhœal arthritis may be

<sup>1</sup> Lancet, London, November 18, 1900.

multiple. A number of joints may be affected simultaneously. In many of the joints the symptoms may consist of only pain and slight tenderness, perhaps slight restriction of motion, but no swelling or effusion into the joint. These symptoms come and go with great rapidity, and are described as "flying pains." This condition is an important one to bear in mind. Dr. Young, in charge of the genito-urinary department at the Johns Hopkins Dispensary, informs me that he observes it frequently in his patients with gonorrhœa. In a careful study of all the cases admitted to the Johns Hopkins Hospital, I find that although the great majority of the cases enter the hospital with only one affected joint (a few, two joints), yet with hardly an exception every patient gives a history of pains, tenderness, and slight restriction of motion in many of the joints at the beginning of the attack; perhaps in a few also a slight swelling. In one or two joints the condition, instead of improving, gradually or rapidly grew worse; the patient on admission to the hospital presented the picture of typical acute arthritis.

It is extremely important during an acute or chronic attack of urethritis, both in men and women, to watch for these joint symptoms. Their appearance should indicate absolute rest in bed and a more energetic treatment of the local gonorrhœic infection, because it has been frequently noted by many observers that a slight trauma or excessive use of any particular joint or joints is followed in the majority of cases by a localization of the infection to that joint leading to an acute arthritis, which if not energetically treated often leads to ankylosis. These fleeting joint symptoms are not infrequently noted when the urethritis is apparently cured, often some years after the primary attack. The diagnosis of chronic rheumatism is usually made, and the proper cause and treatment are lost sight of until one or more joints suddenly become worse; at which time if the effusion is studied bacteriologically the gonococcus will usually be demonstrated. I am surprised to find that Moynihan states as follows: "So far as treatment is concerned, there is little that is new to be said. The main principle is rest. I found great benefit from both mercury and the iodide of potassium and evaporating lotions or tincture of iodine. French surgeons are accustomed to advise incision in these cases, and occasionally this severe procedure may be of value. If the joint be very tense and the pains exceedingly acute, immediate relief is obtained by an incision and the flushing out of the joint with antiseptic fluid." This advice to delay or to operate only in such acute cases will, I am confident, be followed by partial or complete ankylosis in many of the less acute forms, and in many of these acute cases if we wait for these marked symptoms the infection will have so destroyed the synovial membrane that it will be replaced by scar-tissue, and the result will be a more or less impaired joint.

It should be distinctly borne in mind that in every form of acute pyogenic arthritis the inflammation of the synovial membrane tends, if untreated, to reach a stage where, even if resolution takes place, the resulting tissue is chiefly fibrous, and the function in the joint is impaired. To save the synovial membrane one must institute proper treatment before this stage is reached. To open and irrigate such an infected joint at too late a period, in the majority of cases, although it relieves the infection, will *not* save the mobility of the joint.

**The Cultivation of the Gonococcus.** Hugh H. Young,<sup>1</sup> under the title "The Gonococcus: A Report of Successful Cultivation from Cases of Arthritis, Subcutaneous Abscess, Acute and Chronic Cystitis, Pyonephrosis, and Peritonitis," gives us the most complete and best bacteriological study of the gonococcus which has been presented in English. The historical *résumé* is interesting. The demonstration of the gonococcus in any other part of the body except the urethra has only been accomplished since 1892. Although Neisser, in 1879, demonstrated the gonococcus as the cause of the gonorrhœa, it was not successfully cultivated until 1887 by Bumm. In recent years it has been conclusively demonstrated by pure cultures that the gonococcus may be the sole cause of various ascending and metastatic infections. Young, I believe, was the first to demonstrate it in chronic cystitis, pyonephrosis, and diffuse peritonitis. Young reports twenty-three cases in which the gonococcus was found and in the majority of instances cultivated.

In Young's table he records ten cases of arthritis in which the gonococcus was demonstrated: six from the knee-joint; in one of these both knees, one each from the wrist and ankle, one from the tendon sheaths of the ankle-joint, and one from the tendon sheaths of the wrist-joint. Young writes: "All of the cases in which we obtained the culture of the gonococcus were of such severity as to demand arthrotomy, with irrigation of the joint. It is only fair to state, however, that it has been the favorite and very successful practice of Dr. Halsted and his assistants to open, irrigate with bichloride of mercury, and then close the joints with sutures; and that many of the cases operated on were not very urgent, and perhaps might not have been so treated elsewhere; but the good results secured speak for a more frequent performance of arthrotomy." I should like to modify this statement somewhat, in that it was not the severity of the clinical symptoms which influenced us to perform arthrotomy, but rather the

<sup>1</sup> Contribution to the Science of Medicine, dedicated by his Pupils to William Henry Welch upon the Twenty-fifth Anniversary of his Doctorate, Baltimore, 1900, and Johns Hopkins Hospital Reports, vol. ix.

demonstration in the aspirated fluid of the gonococcus, and it is to be noted that in Young's table under the heading "Local and General Symptoms," the terms mild, slight, and subacute are used to indicate that at the time of operation neither the local nor the general symptoms themselves were sufficient to indicate operative interference. Case III., Observation XII., of Young, is an excellent example of gonorrhœal arthritis. The patient was a man, aged twenty-three years. The urethritis was of five weeks' duration. The beginning of the joint infection was eleven days before admission. Both knees, left shoulder and elbow, right wrist, and forefinger were involved. The most marked arthritis was confined to the knees. In both joints the effusion was excessive, but the periarticular œdema not marked. The condition of the other joints was not of a sufficiently high grade to indicate even aspiration. The general symptoms were severe. Demonstrating the presence of the gonococcus by aspiration in both knee-joint effusions, arthrotomy and irrigation were at once performed and the wound closed. It was very interesting to note that on the fourteenth day a subcutaneous abscess developed at the lower angle of the wound on the left knee, and on the eighteenth day a similar abscess on the right knee. In both abscesses Young demonstrated the presence of the gonococcus and no other bacteria. The superficial wounds did not communicate with the joints. Here we have a positive demonstration of the suppuration of a wound due to the gonococcus and without doubt infected during the arthrotomy. The same was observed in Case IV., Observation XIII., of Young, in which a subcutaneous abscess developed in the closed incision made to irrigate the gonorrhœal arthritis in the wrist. In both of these cases the subcutaneous abscess did not complicate the convalescence. In both the functional use of the joints was completely restored. It is important for every surgeon to be familiar with the cultivation of the gonococcus. If in the fluid from an aspirated joint one finds in the cover-slips a coccus morphologically like the gonococcus, it is of itself a sufficient indication to perform arthrotomy and irrigation. If the coccus found in the cover-slips decolorizes by Gram's method, and does not grow on ordinary media, it is pretty positive evidence that the coccus is the gonococcus. In some of Young's cases which I also observed with him we were unable to find the gonococcus in the cover-slip, even after careful search; but Young was able to cultivate it on his special media, while on ordinary media nothing grew. Therefore, there will be cases in which it will be necessary to wait for the result of the inoculation of the special and ordinary media before demonstrating the presence or absence of the gonococcus. I have observed this also in streptococcus infections, especially in the early period of the infection, that we were unable to find any cocci on the cover-slips, but on the

cultures quite a number of colonies of the streptococcus were to be seen after ten to twelve hours in the thermostat.

Granting that the presence of the pyogenic bacteria is a chief indication for operative interference in acute arthritis, and realizing that the earlier the arthrotomy is performed the better the result, one should always be provided with a complete armamentarium of both special and ordinary media. When the cover-slips are negative there will be only but a delay of twelve to twenty-four hours for the positive result from the inoculated media. I would urgently suggest that anaërobic cultures should also be made in the hope that we may demonstrate the presence of such bacteria which only grow in this environment in the cases of acute arthritis in which, so far, bacteriological investigations have been negatived.

Pribram,<sup>1</sup> in his article on acute joint rheumatism, also urges this, and we must not forget Gwyn's very important observation (noted in *PROGRESSIVE MEDICINE* for December, 1899), where, by anaërobic cultures, he was able to demonstrate the bacillus *aërogenes capsulatus* of Welch in the blood during life.

It has been noted in Young's table of the cases of arthritis that hydrocele agar, acetic agar, albuminous urine agar, blood-serum agar, and pig-fœtus and hydrocele agar combined were the various media on which the gonococcus was successfully cultivated by Young, Garrett and Young, Flexner, Follis, and Hagner.

Young writes: "For the most successful cultivation of the gonococcus the presence of albumin, preferably human albumin, is necessary, and various materials and methods of manufacture have been proposed, the means of sterilizing the albuminous fluid being the most important item. For the past three years I have been using hydrocele agar, which has been prepared as follows: The fluid (hydrocele or ascitic) is obtained sterile, the locality of puncture being carefully sterilized by modern surgical methods, the sterile trocar covered at its external end with sterile gauze so as not to be infected by the operator's hand, and the fluid collected in sterile flasks, the sterile stoppers being then replaced. Collecting the fluid in this way we have very rarely had it contaminated, often keeping it several months before using it. This fluid is mixed with ordinary nutrient agar. A number of common agar-slants are put in the autoclave for five minutes; this liquefies the agar and at the same time thoroughly sterilizes the tubes and cotton stoppers. The slants are then put in a water-bath at 55° C., so as not to coagulate the albumin when mixed with the agar. The stopper having been removed from a small flask of hydrocele fluid, the top of

<sup>1</sup> Loc. cit.

the flask is flamed, and the albuminous fluid is then poured into an agar tube (the top of which has also been flamed), in proportions a little more than one to two. It is well to have as much of the hydrocele fluid as the future solidity of the medium will allow. Ordinary agar will allow not quite equal parts of the two. The cork is then returned to the agar tube, which is immediately slanted. When it is desirable to use plate cultures, sterile tubes containing about 7 c.c. of hydrocele fluid are used. These are inoculated and mixed with melted agar slants at a temperature of 40° C., the two being poured separately into a Petri dish. The plate method is not as successful as the slant, presumably because the temperature of 40° C., which is necessary for proper mixture of the liquids, is injurious to the gonococci. I have also found that the gonococci grow most abundantly on slants in or near the liquid which is squeezed out of media and collected in the bottom of the tube.

"There is no doubt but that the gonococci from different sources vary considerably in their cultural characteristics. I have frequently had cultures which maintained a vigorous growth after numerous transplantations. I remember one which was kept alive by students in the laboratory for more than three months; then, again, there are others which grow only two or three times, or, indeed, only once."

This excellent description by Young will make it possible for all of us to have on hand the proper special agar for the cultivation of the gonococcus. At the same time that one inoculated the special media of hydrocele or ascitic agar one should also inoculate the ordinary media, as agar, gelatin, and blood-serum agar.

From the observations of Young and others and the additional remarks made here in the discussion of Young's article, it must not be concluded that one will find the gonococcus in every case of synovitis with effusion associated with gonorrhoeal urethritis. Now that we have such positive culture methods we have frequently demonstrated the sterility of the effusion, even in cases when the effusion is quite cloudy (leucocytes) and contains flakes of fibrin. Such cases have recovered completely after simple aspiration. Now and then a second accumulation has been sterile, although this is not so common. Since Lindemann, in 1892, first demonstrated the gonococcus in pure cultures from the joint, there have been many more reports in which the observer has been unable to demonstrate the presence of the gonococcus than the reverse. This, however, may be due to faulty bacteriology. No surgical report on gonorrhoeal joints will hereafter be at all complete without a bacteriological study with these improved methods of Young.

The older views that purulent arthritis associated with gonorrhoeal urethritis is due to the invasion of other pyogenic cocci than the gonococcus, or that it is a mixed infection, is not confirmed by the more

recent bacteriological observations of Young and others. It has been conclusively demonstrated that the gonococcus in pure culture is the infective agent in the majority of cases or the cultures and cover-slips are negative.

Martel,<sup>1</sup> in an article entitled "Bacteriological Researches on Some Cases of Gonorrhœal Rheumatism and Discussion of the Non-operative Treatment of this Affection," reports eight cases of gonorrhœal arthritis in which the aspirated fluid studied by cover-slip and culture gave negative results. Granting that his bacteriological investigations were true, it is only natural that he should have excellent results from the conservative treatment of simple immobilization. No authority has a right to claim perfect results from the non-operative treatment without a bacteriological report, and it is only in those cases in which the effusion contains the gonococcus that it is fair to compare the operative and non-operative treatments. I am firmly convinced from a large experience that the majority of cases in which the joint effusion contains the gonococcus, that arthrotomy and irrigation practised in the early stages will give the best results.

**Gonorrhœal Arthritis of the Hip.** This, without doubt, is one of the rare joints infected in the course of a gonorrhœal metastatic arthritis. In Prof. Halsted's clinic during the last eleven years there have been about 12,000 surgical admissions. Among these there have been forty-six patients suffering with gonorrhœal arthritis. In two the hip-joint was the seat of the arthritis. In both cases the hip-joint alone was involved, and in both the urethritis was chronic. Case I. (Surgery No. 5481) was a colored man, aged twenty years. He has had a chronic urethritis for three years, but with no joint symptoms. Two weeks ago he fell from his bicycle. He does not remember that he injured any special joint or part of the body. Two days after the accident he noticed pain in the right wrist, a stiff neck, and pain and swelling in the third joint of the left index finger. Two days later he noticed pain in the left hip-joint. He found it difficult and painful to walk, but when he laid down he could not get comfortable except when he flexed the left thigh at the hip. Examination showed that the left leg was held pretty rigid at the hip in a flexed and abducted position. Attempts at motion produced pain. There is an area of tenderness and slight induration in the left groin. The stiffness of the neck, the pain in the right wrist, the pain and the swelling in the finger-joint have disappeared. The slight discharge of pus from the urethra contained a diplococcus, which colored by Gram's method. The patient was placed in bed with the left hip in extension, and the urethra was irrigated; this relieved

<sup>1</sup> Lyon Medical, 1898, No. 33.



the pain somewhat. At the end of six days, the temperature rising the night previous to 103° F., the hip-joint was aspirated under ether anæsthesia. Five cm. of a blood-stained serum were withdrawn from the capsule. When the patient was under the anæsthetic there was very little restriction of motion at the hip-joint. After the aspiration iodoform was injected into the capsule; the hip was put in a plaster cast, with extension on the leg. Cover-slips and cultures on ordinary media were negative. (At this date, May, 1896, we had no special gonococcus media on hand. Previous to this case Flexner had cultivated the gonococcus at the hospital in pig-fœtus agar and hydrocele agar in 1894. It was not until later, in 1896, that Hagner and Young<sup>1</sup> began the successful cultivation of the gonococcus.) The night after operation, the patient said, was the most comfortable since his admission, and from this time on recovery was uninterrupted, and there was no fever. Three weeks later, without ether, the joint was again aspirated, with negative result. Iodoformized oil was again injected. At the end of four weeks the extension was removed and the patient was allowed to get up and walk. The affected hip was fixed in a plaster cast. He was discharged from the hospital three months after admission. At this time the urethral discharge had ceased; the patient walked with the aid of a cane, but complained of no pain or tenderness in the hip-joint. There was, however, slight restriction of motion. Examined two months later, the patient expressed himself as being perfectly well with the exception of a slight stiffness of the left hip-joint, and on examination one finds that flexion and abduction were somewhat limited.

Case II. (Surgery No. 6274) was a male, aged twenty-eight years. He gave a history of gonorrhœa of one year's duration, followed two and a half months later by an adenitis in the right groin, which suppurred, but healed quickly. There have been no joint complications. The patient stated that the discharge from the urethra had ceased. Five days after a severe twist in the right hip the patient was seized with a severe pain in the right hip while sitting quietly in the chair, and stated that for an hour and a half the pain was so intense that he cried out, and the physician who was called to see him injected morphine. Since this first attack he has suffered no pain except at attempted motion at the hip-joint. He has been unable to bear any weight on this limb. In a few days he noticed that the right leg was longer. When lying in bed the leg is more comfortable in a position of flexion and abduction. Three days after the onset of the arthritis of the hip without apparent cause the patient noticed a discharge from the urethra, which

<sup>1</sup> Loc. cit.

he emphatically stated had not been present for some months. He also stated that there had been no other painful joint. On examination one found that the right leg was flexed, abducted, and rotated out at the hip, and any attempts at motion produced pain. The treatment was extension in bed from February 12th until March 6th. At this time the patient was placed under ether, and it was found that the deformity and fixation of the hip had been almost entirely due to muscular spasm. The deformity was easily reduced and the hip placed in plaster. After ten days the plaster was removed. There was no restriction of motion, no deformity, and no pain. The urethral discharge was yellow pus. The examination of the cover-slip showed cocci inside and outside of cells morphologically like gonococci; but these did not decolorize by Gram's method, and on Hagner-Young albuminous urine agar did not grow like the gonococcus, but grew on other media and were demonstrated to be the staphylococcus pyogenes albus. While in the hospital a careful temperature-chart showed no fever. The patient was discharged at the end of thirty-one days, well, and a letter received from him one year later informed us that he has had no other attack and the functional use of the hip-joint is perfect. Whether this should be considered a gonorrhoeal arthritis is a question. Clinically it was the picture of acute arthritis of the hip; the only portal of entrance for the metastatic infection was the urethra. Here careful bacteriological study demonstrated not the gonococcus, but the staphylococcus pyogenes albus. This might have been the cause of the arthritis, or it is quite possible we may have overlooked the presence of the gonococcus in the urethra on account of the predominant staphylococcus albus.

F. Duplant and M. Péhu, of Lyons, report two cases of acute arthritis of the hip associated with urethritis, in which, without doubt, the gonococcus was found in the urethral discharge. One case was a male, aged twenty-six years, and the other a female, aged twenty-one years. In both the hip was the only joint involved. In the first case recovery was rapid and complete after a few weeks' treatment in extension. In the second case (the woman) at the end of one year the motions of the hip-joint were still very much restricted. In both cases the symptoms of pain, slight induration, and swelling below Poupert's ligament and in Scarpa's triangle were present, similar to the first case just reported. In neither of these two cases was aspiration of the joint for treatment or bacteriological investigation instituted. The authors state that they believe in such a condition the aspiration of the joint would be difficult. I cannot agree with them. The result of my first case here reported demonstrates its ease and happy result, although there was but very little effusion. In my second case there was no indication. In PROGRESSIVE MEDICINE for December, 1899, p. 198, I wrote:

"One should not hesitate, however, to open and irrigate the hip-joint through an anterior incision if the signs of distention of the capsule were present when previous aspiration revealed the presence of the gonococcus in the effusion." So far I have had no experience in acute arthritis of the hip, with effusion, to institute this treatment except in tuberculosis, where recent experience has most satisfactorily demonstrated the happy result.<sup>1</sup>

Duplant and Péhu find in a study of the literature that very few cases of gonorrhœal arthritis at the hip are reported. Philippi, 1893, in his thesis, reports one case; Mauclaire<sup>2</sup> reports three cases in a series of thirty of purulent arthritis. In 1896, Griffon demonstrated by bacteriological study the presence of the gonococcus in the hip-joint and other organs in a new-born child. No reference is given to this very important observation. M. C. Audry, in his most complete thesis, agrees with Lagrange that gonorrhœal arthritis of the hip is more frequent than the record would show, because it is mistaken for tubercular arthritis or arthritis following puerperal infection, which in many cases is due to the gonococcus. In the literature from 1898 up to the present time (August, 1900) I am unable to find any other cases of gonorrhœal arthritis of the hip-joint.

From the moment of first symptom of pain, tenderness, or restriction of motion at the hip-joint, with or without the positive evidence of a gonorrhœal urethritis in the male or the female, the patient should be placed at once in absolute rest in bed, an extension applied to the affected limb, with the addition of some fixation of the hip-joint itself. The presence and continuation of fever, the non-disappearance of the pain and tenderness in the groin, or the appearance of a distinct fulness in the groin should indicate aspiration of the hip-joint capsule at once. The bacteriological study of the fluid should indicate arthrotomy, as already described. Such early orthopedic treatment followed when indicated by the bacteriological findings, by arthrotomy and irrigation, should lead to happy results in every case.

### ACUTE JOINT RHEUMATISM. (RHEUMATISMUS ARTICULARIS ACUTUS.)

A. Pribram<sup>3</sup> contributes a monograph, and I should infer from the excellent review<sup>4</sup> that it is the most complete résumé of the subject up to

<sup>1</sup> Johns Hopkins Hospital Bulletin, January, 1900.

<sup>2</sup> Arch. gén. de Méd., 1895.

<sup>3</sup> Vienna, 1899. Alfred Hoelder. Spezielle Pathologie und Therapie von Nothnagel, Bd. v., Theil i.

<sup>4</sup> Centralblatt f. die Grenzgebiete der Medizin und Chirurgie, Bd. ii., Nos. 17 and 18, p. 748.

date. Nevertheless, he leaves us still in the dark as to the pathogenesis of the disease and the treatment. He believes that perhaps more frequent anaërobic cultures from the blood and the joint effusions may demonstrate specific but yet unrecognized bacteria, and, if this fails, the cause may be found in some chemical disturbance, especially in the blood. All this, however, is left for future investigations; he has no positive data at present.

Pribram teaches that the complex of symptoms of acute joint rheumatism should be considered to be a distinct disease, although there are many conditions produced by various infections whose clinical appearance are very much similar, but which should be differentiated, such as the polyarthritides due to the gonococcus, the pneumococcus, streptococcus, and the staphylococcus, or associated with infectious diseases like scarlet fever, dysentery, typhoid, etc. These forms of polyarthritis may be primary, or in some cases they may be the secondary invaders, in which the primary condition was an acute joint rheumatism. Unquestionably, in patients suffering with acute joint rheumatism the affected joint's resistance to secondary infection is lower, but in those cases in which the different bacteria have been found they should not be considered the cause of the disease. In the great majority of observations cultures from the joints and the blood in acute joint rheumatism are sterile; in those cases in which bacteria have been found the infection should either be considered a secondary one to acute joint rheumatism or that the disease was from the first a polyarthritis due to the infectious organism demonstrated in the culture.

Pribram admits the possibility of osteomyelitis and periostitis in acute joint rheumatism, but states the question is not yet settled; the question to be settled is the possibility of a definite periostitis or osteomyelitis being produced by the specific agent in acute joint rheumatism (bacterial or chemical), or whether it is not always due to some secondary infection. If we agree with Pribram we must separate true acute joint rheumatism from all other forms of polyarthritis and restrict this term to this disease, and not use the words rheumatism, rheumatoid, or rheumatic with any other form of polyarthritis, but designate them as arthritis or polyarthritis, gonorrhœic, and so forth. Pribram states, both from his own observations, which are large, and from the literature, that the skin complications in acute joint rheumatism are relatively rare. The erythema and ecchymosis about the joints are not common; this, in the past, has been considered quite a diagnostic sign in acute joint rheumatism, but if Pribram's observations are correct they cannot be considered so any longer. When present, he believes they are always due to distinct diapedesis; but their presence does not increase the gravity of the prognosis. These areas of minute hemorrhage must be differentiated

from Henoch's purpura, which, as a rule, begins in the lower bowel and the kidney and ends with a nephritis, and, as this disease is frequently associated with joint symptoms, the difficulty of the differential diagnosis is increased.

This erythema and ecchymosis about joints are also observed in other grave joint infections. I observed in two cases of subacute arthritis of the ankle, in which in the beginning of the attack a number of joints were involved, areas of ecchymosis about the swollen ankle-joints at this time influenced us in the diagnosis of rheumatism and delayed the operation, which was later forced upon us by the increasing swelling and œdema; in both cases we found a perforation of the posterior capsule of the ankle-joint, with a collection of pus in the space between the joint and the tendon of Achilles. In one case the cultures were sterile, but the histological picture showed tuberculosis of the synovial membrane and the lower end of the tibia; in the other case we found the gonococcus, although the patient denied urethritis, and the examination of the urethra was negative.

These observations should influence us not to put too much stress on areas of ecchymosis in the œdematous tissue about joints, as they are conditions present in a number of diseases.

### ARTHROPATHIES ASSOCIATED WITH NERVOUS LESION.

In *PROGRESSIVE MEDICINE* for December, 1899, the arthropathies associated with posterior sclerosis (Charcot's joints) and syringomyelia were considered. Recent literature is rich in the study of these cases, a knowledge of which is as important to the surgeon as to the neurologist.

**Charcot's Joint.** In the past year I can find but one additional reference to resection for tabetic arthritis. Alexander B. Johnson,<sup>1</sup> of New York, reports one case before the New York Surgical Society. The history of the patient is of interest because the arthritis of the knee which followed a slight injury was for some time the only apparent symptom, and was considered and treated at first as traumatic synovitis, and later, as there was no improvement, it was thought to be tuberculosis. The patient was a married woman, and when admitted to the Roosevelt Hospital, eighteen months after the beginning of the arthritis, showed the characteristic signs of posterior sclerosis. Dr. Johnson excised the knee-joint under ether. The pathological changes are described as follows: the effusion was brownish and semi-transparent; the articular cartilage was in a condition of fibrous degeneration; at the border of the cartilage, on the patella, there were numerous cartilaginous and

<sup>1</sup> *Annals of Surgery*, July, 1900.

bony plates; the synovial sac beneath the quadriceps muscle was dilated; the surface of the synovial membrane was studded with small calcareous plates; it was brownish-red in color and rough. In the internal condyle of the femur there was a deep cavity (one inch in diameter); this cavity was occupied by a projection from the corresponding head of the tibia. The cavity was lined by rough, fibrous tissue. The lateral ligaments of the knee-joint were greatly relaxed; the outer semilunar cartilage was normal, the inner was replaced by a regular mass of fibrous tissue infiltrated with calcareous salts. The outer condyle of the tibia was covered with rough, fibrous cartilage, and from its posterior border an osteophyte projected. There were no areas of denuded bone. On sections of the condyles of the femur and head of the tibia there were areas of soft bone and eburnated bone. The external wound healed, but at the end of twelve weeks there was no bone union. The X-ray photograph showed no evidence of bone formation after four months. The patient was able, however, to get about with comfort with the leg fixed in plaster. In the discussion Dr. Whitman stated that in one case under his own observation union after resection had not taken place. Dr. Willy Meyer has had one successful case after excision; but Dr. Ellsworth Eliot's case of resection was unsuccessful. My own case<sup>1</sup> healed with osseous union.

Considering the entire experience reported in the literature, the probabilities of union of the bone after the resection of the knee-joint are fair. Excision of other joints give, on the whole, better results. Amputation, when the arthropathy was very advanced, relieved the patients of much discomfort. The wounds of the soft parts heal as well as in any other class of patients, so that, on the whole, operations for a Charcot's joint are justified.

**Arthropathies in Syringomyelia.** In continuation of what was written in *PROGRESSIVE MEDICINE* of December, 1899, I find that N. A. Sokolow<sup>2</sup> calls attention to the frequent occurrence of shoulder luxation in syringomyelia. He has recently observed two cases which at first appeared to be purely traumatic, but on closer examination the typical picture of syringomyelia was evident. He states that one should always think of the possible presence of syringomyelia in every luxation of the shoulder, and during the reduction the greatest care should be practised, because, on account of the fragility of the bone, rough manipulation may produce a fracture. Gnesda<sup>3</sup> reports a case of arthropathy

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1899, p. 201.

<sup>2</sup> *Wrathe*, 1899, No. 27. *Centralblatt f. Chirurgie*, 1900, Bd. xxvii., No. 9, p. 243.

<sup>3</sup> *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 1899, Bd. iv., p. 733; *Centralblatt f. die Grenzgebiete der Medizin und Chirurgie*, 1899, Bd. ii., No. 33, p. 930

of the shoulder-joint, which is of especial interest because it was the first symptoms of syringomyelia.

The most extensive and important contribution to this subject during the past year is a second communication by N. A. Sokolow<sup>1</sup> (the German spelling of this name is Sokoloff). This article is a continuation of his first communication,<sup>2</sup> in 1891. In his first article all previous joint arthropathies of his own and those to be found in the literature are reported. Since Sokolow, Graff<sup>3</sup> has added twelve new cases. Schlesinger, in his monograph<sup>4</sup> in 1895, was able to collect sixty-three joint arthropathies (10 per cent. of all cases of syringomyelia).<sup>4</sup>

A knowledge of joint arthropathies in syringomyelia is of great importance to the surgeon in the differential diagnosis, especially in the early stages, when the symptoms and the cause of the arthritis are obscure. Sokolow adds eight new observations. In eight patients ten of the large joints were involved; five times the elbow; twice the shoulder-joint and wrist-joint, and once the sternoclavicular joint. The situation of the arthropathy in these cases to the upper extremity is that which distinguishes the arthritis of syringomyelia from those of tabes dorsalis. In the former in 80 per cent. of the cases the upper extremity is involved, while in the latter in about the same percentage the lower extremity. As a rule, the course of the arthritis in syringomyelia is more gradual and of much longer duration than in tabes. The clinical picture of both arthropathies is very much alike. Effusion, relaxation of the capsule and tendons of the joints allowing increased mobility, œdema of the periarticular tissue, tendencies to dislocation are common to both. Destruction of the joint cartilage, on account of pressure, is more common in the lower extremity, and therefore in tabes. An enlargement of the bony ends of the affected joint is more marked and more common in syringomyelia. The formation of sequestrum has also been observed more frequently in the syringomyelia arthropathies. Sokolow records, in addition to the arthropathies, two cases of fracture of the ulna near the affected joint. In the past this has been considered a rare condition, but Sokolow's observations would indicate that it is not quite so uncommon. Fracture associated with tabetic arthritis is more rare. In Sokolow's experience the accidental complications associated with syringomyelia and its arthropathies are not serious. Infected wounds heal; even the pyogenic infections of the diseased joint (a rare complication) are relieved by proper treatment; fractures heal, and any necessary operation may be performed without fear of necrosis of the bone or non-healing of the bone or of

<sup>1</sup> Deutsch. Zeitsch. f. Chir., 1899, Band li., p. 506.

<sup>2</sup> Beiträge zur Chir., Band 10.

<sup>3</sup> Ibid., Band xxxiv.

<sup>4</sup> Die Syringomyelie.

the soft part ; this is also true in tabes. In Sokolow's experience these arthropathies, although not cured, respond to proper treatment. Aspiration of the fluid to relieve the tension, and support of the joint with some form of orthopedic apparatus or bandage, generally prevents the re-formation of the effusion and extra-articular swellings and aids in the functional use of the limb. A short review of the more important points, especially in regard to the arthropathies in Sokolow's<sup>1</sup> eight cases, with a reproduction of some of his excellent photographs, will give one an excellent idea of the joint complications.

Case I. Arthritis of the elbow, with luxation of the head of the radius and fracture of the diaphysis of the ulna—syringomyelia symptoms, scoliosis, characteristic changes in the fingers, thumbs, and partial pain anæsthesia. The patient was a woman, aged forty-three years, and claims to have had no previous illnesses except, a number of years ago, pain and swellings in various joints, and during the last six months pain and slight crepitation in the hand. She sought advice at the clinic, however, for pain and swelling in the elbow-joint following a slight trauma three months ago. On examination the typical picture of a marked arthropathy was present. The elbow-joint was greatly enlarged ; one could feel the head of the dislocated radius and the crepitus of the fractured ulna. There was increased lateral motion and fluid in the joint. Definite symptoms pointing to a syringomyelia were noted. Fixing the arm in plaster, the fracture healed solidly, and the swelling of the joint decreased so that when the patient was discharged, five months later, she had quite good functional use of the arm. She was advised to continue the use of a supporting orthopedic apparatus. Although the patient's attention was not called to the affected elbow until three months ago, after the trauma, the arthropathy was without doubt of longer duration. Trauma probably increased the effusion and perhaps fractured the ulna.

Case II. Arthritis of the elbow, with posterior dislocation ; history of repeated freezings of the fingers, deformities of the fingers, and changes in the nails, scoliosis, increased sensibility to pain, and thermo-anæsthesia of the upper extremities and the posterior surface of both thighs. This patient was a man, aged forty-three years. The arthropathy of the right elbow has been present at least twenty years. He has been able to use the arm, and only sought advice at the clinic because, six months ago, and especially two days ago, following injury, there was increased swelling and pain. Fig. 54 is a good illustration of the condition, showing a great enlargement at the elbow, with dislocation and atrophy of the muscles of the arm and forearm. There is

<sup>1</sup> Deutsch. Zeitsch. f. Chir., Band li., 1899.



increased mobility and a marked exudate, with enlargement of the ends of the bones, especially the olecranon, head of the radius, and external condyle of the humerus. No crepitation. Aspiration removed considerable fluid which was at first clear and then bloody. The patient refused treatment and left the hospital. The duration in this case of at least twenty years, and the excellent use the patient had of the arm, even in spite of the extensive arthropathy, is interesting.

FIG. 54.



Arthropathy of elbow in syringomyelia. Sokolow's case.

Case III. Slight arthropathy of the right shoulder; marked arthropathy of the left elbow; deformity of the fingers and changes in the nails; scoliosis; burns reduced sensibility to pain, and thermo-anæsthesia of the upper extremities. This patient was fifty-two years of age, and sought advice on account of pain and swelling of the right shoulder, which followed a strain a short time ago. One found a swollen shoulder, with no restriction of motion. Head of the humerus distinctly enlarged; slight crepitation, but there were no loose bodies to be felt. There was evidence of extravasation of blood in the tissues about the joint, and the veins in the skin were enlarged. This arthropathy, according to the patient, was of short duration. He did not seek advice at the clinic for the condition of the left elbow, which was of much longer duration and the arthropathy much more pronounced.

The elbow was swollen, with marked atrophy of the muscles, enlargement of the ends of the bone, and increased lateral motion. However, he suffered from no pain in the elbow and was able to use the arm. He refused treatment. Some months later the patient died, and at the autopsy a definite area of syringomyelia was found. As Sokolow and other observers have demonstrated, in all cases the syringomyelia, either by clinical signs or confirmed by autopsy, always occupies a position in the cord in direct relation to the arthropathies.

Case IV. Arthropathy of the left elbow and sternoclavicular joint; asymmetry of the face; scoliosis; slight nystagmus; pain and thermo-anæsthesia; circumscribed necrosis of the lower end of the humerus in the form of small sequestrum, resection of the joint without narcosis. This patient

FIG. 55.



Arthropathy of elbow in syringomyelia.  
Sokolow's case.

is the youngest in the group of eight cases—twenty-five years old. The disease seemed to be associated with an injury to the spine six months ago. The patient sought advice at the clinic because of the weakness of his left hand and intense headache. At the examination definite, symptoms of syringomyelia with arthropathy in the two mentioned joints were found. Fig. 55 is an excellent illustration of the gross appearance of the joint. This patient was a remarkably well-developed and nourished man. He complained of no pain in the elbow or sternoclavicular joint, although there were fistulæ present and the evidence of supuration. The usual gross pathological picture was present. While in the hospital a number of small operations were first performed in incising the fistula and for small areas of circumscribed

gangrene of the skin about the elbow-joint. The elbow-joint became infected, and excision without narcosis was performed. (In PROGRES-

SIVE MEDICINE for December, 1899, I reported a case in which I excised the knee-joint for tabetic arthritis under local anæsthesia.) Sokolow is of the opinion that the circumscribed areas of necrosis in the bone in these arthropathies are due to the same trophic cause which produces these circumscribed gangrenous areas of the skin and the other pathological changes. He does not agree with Schlesinger's views that the necrosis is due to destruction of the periosteum by the inflammatory process.

FIG. 56.



Arthropathy of wrist in syringomyelia. Sokolow's case.

Case V. Arthropathy of the right carpus, with marked muscular atrophy of the right hand; scoliosis; hallux and pes valgus; reduced sensibility to pain and atrophy of the deltoid and interosseous muscles. This patient was a woman, aged fifty-three years, and sought advice at the clinic because of pain in the knees, dyspnoea, palpitation of the heart, and headache. She had been treated in the hospital seven years before for pain and swelling of the joints of one month's duration. The arthropathy of the right carpus had been present thirty-five years. The first attack consisted of swelling of many joints; the swelling, however, of the right carpal bones remained, and has increased during these thirty-five years, although she has been able to work and has suffered

no pain. Fig. 56 is a good illustration of the condition. Here we see marked deformity and dislocation, and on examination the radius and ulnar bones are normal, but all the carpal bones are enlarged. Changes due to chronic rheumatoid arthropathies may be present, but the clinical picture and the history are positive as regards the syringomyelia.

In Case VI., in addition to the arthropathies of the elbow-joint and the dislocation of the head of the radius, there was a fracture of the ulna, with fibrous union. The patient was sixty-two years of age, and the arthritis of the elbow had been present sixteen years without trauma. When the patient was admitted to the hospital, in addition to the fracture, there was a circumscribed area of gangrene on the skin. This, with the fracture, healed under proper treatment.

Case VII. Arthritis of the left shoulder-joint, dislocation of the humerus, marked effusion; pain and thermo-anæsthesia in the area of

FIG. 57.



Arthropathy of shoulder [in syringomyelia.  
Sokolow's case.

the arthropathy; circumscribed necrosis of the head of the humerus in the form of small sequestra. This patient was a man, aged thirty-seven years. During the last fifteen years he has had three bad falls from his horse. For seven years he has had remittent attacks of vertigo; otherwise he has been in apparently good health and able to do his work. Without apparent cause, about three weeks ago, he felt pain in the left shoulder, which was followed by swelling. This was the first time his attention was called to the shoulder-joint. Fig. 57 is a good illustration of the gross appearance of the shoulder arthropathy. The head of the humerus is very much enlarged, and there is a good deal of effusion in the joint. The skin over the shoulder is smooth and glazy; the superficial veins are dilated. In this case the appearance of the arthropathy was unusually rapid—an excep-

tion in syringomyelia. Unquestionably there were pathological changes of much longer duration before the trauma, followed by effusion, which brought on acute symptoms and drew the patient's attention to the joint.

Case VIII. is one of the right wrist-joint. The arthropathy was slight. There was, however, marked deformity and contractures of the fingers, with degeneration of the nails. There had been repeated inflammations of the fingers (panaris), which had not gone on to necrosis. The skin of the hand was covered with areas of callus. This case is a good example of the diagnostic value of relapsing panaris as a symptom of syringomyelia; especially is this a help when there are no joint symptoms. It is interesting to note in these eight cases that the effusion into the joint in one or two instances was the first symptom of trouble. This will be discussed later under the next subject.

It is unfortunate that Sokolow has seen his cases so late in the disease. He states that the patients were Russian peasants who pay very little attention to the condition of their bodies until the disease is so far advanced that they are unable to do any work. These cases are a splendid illustration of the long duration of the arthropathies in syringomyelia, and how frequently the function of the limb is pretty well preserved. Pain is not a characteristic symptom unless there is great tension from effusion and periarticular oedema generally associated with trauma. The presence of a fracture is seldom observed by the patient, and when dislocation is present the active or passive mobility of the joint is not much restricted; this is due to the extensive relaxation of the ligaments.

### **HYDROPS HYPOSTROPHOS AND HYDROPS ARTICULORUM INTERMITTENS.**

In the recent literature on diseases of the joints an article of some thirty pages by Herman Schlesinger,<sup>1</sup> of Vienna, has perhaps been the most interesting and instructive, not only because the disease is an uncommon one, but chiefly because in the differential diagnosis a knowledge of the various joint diseases is reviewed. Schlesinger gives sixty references to the literature, and in reporting two cases in his own observations he considers in detail forty-seven cases which he has gathered from the observations of others. After his careful study he feels convinced that the condition described under the name hydrops articulorum intermittens (or intermittent joint hydrops) should be classed among the neuroses with angioneurotic oedema.

<sup>1</sup> Mitteilungen aus den Grenzgebieten der Med. und Chir., 1899, Band I., Heft 3, p. 441.

The chief interest in this condition is before the diagnosis is made because a positive diagnosis depends upon the positive exclusion of all other conditions which may give rise to joint effusions.

Intermittent joint hydrops is a condition in which there is swelling due to effusion or periarticular œdema of one or more joints. In the first instance the swelling may follow a slight trauma ; frequently there is no history of trauma. The swelling may attack any joint or only one joint. The same joint may be affected through the entire course of the trouble, or a number of joints following each other in rotation. During the attack the joint is simply swollen, and there may be a little pain. Without any apparent reason the swelling disappears, to return at intervals of weeks, months, or years, and then to spontaneously disappear. Seldom is the skin reddened, and, as a rule, there is no fever. Between the attacks the joint is perfectly normal, and there is no loss of function. The interval may be regular, and, as a rule, during the first series of attacks the interval is quite regular ; later the intervals may become irregular. The knee-joint is the most frequent one to be attacked, although no joint is exempt.

**CLASSIFICATION.** This condition should be divided into two classes — symptomatic and idiopathic. To the latter group belong the cases in which the cause of the joint effusion after most careful study cannot be associated with any special condition, except, as Schlesinger concludes, to a neurosis similar to angioneurotic œdema.

**Symptomatic Hydrops Articulorum Intermittens.** In this group the joint effusion or periarticular œdema (more commonly joint effusion) is a secondary symptom. In two instances von Brinker and Nicolaysen noted it associated with *acute splenic tumor*, both conditions disappearing at the same time. In Nicolaysen's case the disappearance of the splenic tumor and the joint hydrops was associated with the therapeutic use of arsenic. In Moore's case the splenic tumor remained unchanged during the interval between the joint effusion. Quinine had no effect on either condition.

A few cases have been observed in *malaria* ; it is, however, very rare. Mannaberg, in his classical monograph on malaria, states that very little is known of joint affections during malaria ; but Fayser, in his observations in India, states that rheumatic affections without endocarditis appear quite frequently in malaria. Verneuil also records joint neuralgia in malaria.

**OSTEOMYELITIS.** The possibility of intermittent joint hydrops due to chronic osteomyelitis at the epiphyseal end of the diaphysis must always be borne in mind. In Sarre's case, which for some time was considered an idiopathic joint hydrops, an operation at a later interval demonstrated an abscess in the external malleolus and unquestionably the

cause of the intermittent hydrops of the ankle. I have observed three or four cases of remittent joint effusions associated with chronic osteomyelitis. In one case on aspiration we got a few colonies of the staphylococcus pyogenes aureus, but the relief of the bone affection within twenty-four hours checked the recurrence of the effusion. There was no further joint trouble.

**GONORRHOEA.** As already discussed, intermittent joint effusion is not uncommon in gonorrhœa. More frequently it is simply slight pain in the joint, but not infrequently there is either effusion or slight periarticular œdema, which comes and goes at irregular intervals, but seldom becomes a serious arthritis. There are no records of aspirations and cultures in such cases.

**INFECTION.** Intermittent effusions in or about the joints are not uncommon in some infections. Such a condition, however, should be distinguished from acute joint rheumatism.

**AUTO-INTOXICATION.** Ferre is of the opinion that many cases of intermittent joint effusions are the expression of a slight auto-intoxication. This is the French view of many cases, but it is not yet proven; but Schlesinger believes there is much in favor of this view.

**PRELIMINARY STAGE TO A PERMANENT CHRONIC ARTHRITIS.** Intermittent joint swellings may be the first symptoms of a more permanent chronic arthritis, especially the chronic rheumatoid arthritis and the various arthropathies such as are associated with tabes dorsalis and syringomyelia. Ferre, Hartmann, Moore, Nasse and others have observations to this effect.

**URIC-ACID DIATHESIS.** Cases of intermittent joint swellings have been recorded clinically to be associated with the uric-acid diathesis, as Grendidier's case.

**LUES AND TUBERCULOSIS.** Friedenburg has recorded cases of intermittent joint effusions in syphilis and Colonna in tuberculosis. The latter observation of Colonna is a very important one and should be constantly borne in mind. Recently, in looking over a number of cases of tuberculosis, especially of the knee, there were quite a few cases in which intermittent joint effusions were present during the early months of the disease, which later developed into tubercular arthritis, confirmed by operation. In these cases it is not uncommon in the interval to have no joint symptoms. Krause states that the majority of cases of tubercular arthritis began with a joint effusion, the primary tubercular synovitis almost always, and when synovitis is secondary to the tubercular osteomyelitis of the epiphysis this joint effusion may be the first symptom of the disease. Schlesinger does not call attention to the cases of intermittent joint effusion associated with loose cartilage, with dislocated semilunar cartilage, and with

lipoma of the joint. This was thoroughly discussed in *PROGRESSIVE MEDICINE* for December, 1899. König especially draws attention to the intermittent attacks of joint effusion, usually, however, associated with a good deal of pain and restriction of motion in the history of cases in which a loose cartilage has been found later in the joint.

Given, therefore, a case of joint effusion of one, especially, or even more joints at the first or at a remittent attack, all these possibilities must be borne in mind before the diagnosis of idiopathic hydrops articu-lorum intermittens can be made.

**Idiopathic Hydrops Articulorum Intermittens.** Schlesinger has collected fifty-five cases, including his own two. In fourteen of these cases, however, the condition may have been symptomatic. In forty-one cases the condition of a secondary arthritis could practically be excluded, and so belong to the idiopathic group. One of his own cases was not typical. The other case was a typical one. Of the 49 cases in which the location is noted, of the 13 classified symptomatic, in 8 one knee-joint was involved, in 3 both knee-joints, in 1 case the knee-joint and other joints, and in 1 case other joints. Of the 35 cases classed as idiopathic 12 involved a single knee; 15, both knees; 7, knee-joint and other joints, and 2, other joints only. One or both knees were, therefore, involved in 94 per cent. of cases. The knee-joint is, therefore, seldom free.

**SEX.** Of the 11 symptomatic cases 7 were in males and 4 in females. Of the 38 idiopathic cases 17 were males and 21 females; total, 49 cases, 24 males and 25 females. The following table shows:

#### MALES.

|                                 | Idiopathic. | Symptoms. | Total.   | Per cent. |
|---------------------------------|-------------|-----------|----------|-----------|
| Up to 10 years of age . . . . . | 0           | 0         | 0        | 0         |
| " 20 " " . . . . .              | 4           | 1         | 5        | 26        |
| " 30 " " . . . . .              | 3           | 2         | 5        | 26        |
| " 40 " " . . . . .              | 5           | 2         | 7        | 37        |
| " 50 " " . . . . .              | 1           | 1         | 2        | 11        |
| " 60 " " . . . . .              | 0           | 0         | 0        | 0         |
| Not given . . . . .             | 4           | 1         | 5        |           |
|                                 |             |           | <hr/> 24 |           |

#### FEMALES.

|                                 | Idiopathic. | Symptoms. | Total.   | Per cent. |
|---------------------------------|-------------|-----------|----------|-----------|
| Up to 10 years of age . . . . . | 1           | 0         | 1        | 4         |
| " 20 " " . . . . .              | 7           | 1         | 8        | 33        |
| " 30 " " . . . . .              | 10          | 1         | 11       | 46        |
| " 40 " " . . . . .              | 2           | 1         | 3        | 13        |
| " 50 " " . . . . .              | 0           | 0         | 0        | 0         |
| " 60 " " . . . . .              | 1           | 0         | 1        | 4         |
| Not given . . . . .             | 1           | 0         | 1        |           |
|                                 |             |           | <hr/> 25 |           |



It is to be noted, therefore, that in men the most common age is between thirty and forty years and in women between twenty and thirty years. This is not an uncommon age for many other joint conditions, even tuberculosis, and does not help much in the diagnosis. In women the attack of joint effusion occurs frequently during menstruation, but the advent of pregnancy will interrupt the attacks, which will again appear after delivery. Attacks generally disappear and seldom appear after the menopause.

**The Relation of Hydrops Articulorum Intermittens to Other Neuroses.** Other secondary nervous symptoms are not uncommon in association with intermittent hydrops, such as epilepsy, progressive general paralysis, hysteria, exophthalmic goitre, and tachycardia. Organic heart lesions are seldom associated with intermittent hydrops. Schlesinger then records many individual cases of various observers in which previous to the development of intermittent hydrops various nervous manifestations have been observed. The presence of atrophy of the muscles above the affected joint is almost constant in intermittent hydrops; but, as Schlesinger proves, there is no indication that this atrophy means pathological changes in the joint. However, after the attack the atrophy and weakness of the muscles disappear. It is not uncommon to find associated with atrophy twitchings of the muscles.

**Relation of Idiopathic Joint Effusion to Acute Circumscribed Œdema of Quinke.** Schlesinger, in going over the literature of these two subjects, finds a distinct relation between the two conditions, and feels that the joint effusion is perhaps a manifestation of circumscribed œdema, which, when situated in the joint, shows itself as an intra-articular or periarticular effusion. In both conditions the œdema is intermittent. In both conditions there are no local or general symptoms of inflammation. In both between the attacks the parts are normal. There are no gross or apparent microscopical pathological changes.

**Hydrops Hypostrophos Tendo-vaginarum.** This term is used by Schlesinger to describe a number of conditions in addition to hydrops articulorum intermittens and acute circumscribed œdema of Quinke, because of the similarity of symptoms and localization. For example, the following conditions:

1. Relapsing œdema of the lids.
2. Some form of remittent nasal catarrh.
3. Intermittent swelling of the tendon sheaths, cases of nervous ptosis.
4. Some cases of pseudocroup.
5. Progressive asthma.
6. Nervous polyuria and diarrhœa and acute chemosis.

These conditions, along with intermittent joint effusions, have the following similar symptoms :

1. They occur in nervous individuals without special cause.
2. There may be mental or physical trauma in which the cause is slight and the result pronounced.
3. The sudden appearance of the condition.
4. Its marked periodicity.
5. Its relation to menstruation and pregnancy.
6. The normal condition of the parts between the attacks.
7. The disappearance of the condition, even for years, with sudden remittance.

In all of these conditions there is oedema of the tissues, which appears suddenly, lasts a certain length of time, and disappears, to appear again. The intervals passed may be regular, then irregular. Locally there is no evidence of inflammation and there is no fever. Between the attacks the part is normal. The literature of *hydrops articulorum intermittens* and the number of cases point to the relation between this condition and the above conditions grouped under *hydrops hypostrophos*, especially in those cases of intermittent joint hydrops where the swelling is chiefly periarticular oedema and not effusion. Schlesinger then records some of these cases in detail, and on the other side, in the literature of the conditions grouped under the term *hydrops hypostrophos* it is not uncommon to find recorded joint affections similar to intermittent joint effusion. According, therefore, to the view of Schlesinger, *hydrops articulorum intermittens* is simply a form of angioneurotic oedema localized in the joint. Therefore, Schlesinger advocates the term *hydrops hypostrophos articulorum*.

**TREATMENT OF INTERMITTENT JOINT HYDROPS.** In the first place it is of the greatest importance to exclude the symptomatic forms—those associated with osteomyelitis, urethritis, malaria, uric-acid diathesis, tuberculosis, lues, etc. This differential diagnosis is frequently a difficult one, especially in the early stages, so that surgeons should be very careful not to make too positive a diagnosis.

In the idiopathic form there is not much to be said in favor of treatment. As regards drugs, arsenic has given the best results. Locally during the attack the conservative treatment is rest, ice, heat, and bandages. Surgically, the effusion if producing great tension should be aspirated, and in some instances injections have been used. Arthrotomy and irrigation have also been used. There is nothing, however, to indicate that arthrotomy and irrigation are even justifiable. Aspirations of the effusion relieve the tension, but probably have no effect on the disease itself. Following the aspiration compression should be used. The disease in many cases disappears spontaneously and does not remit.

To the surgeon the appearance of a joint effusion brings up at once a difficult question of diagnosis. If the trauma has been severe, effusion is easily explained. If there has been a slight trauma or no trauma, a great many conditions, some very grave ones, should be thought of. Unquestionably, in every case the joint should be aspirated for a bacteriological study. A sterile fluid still leaves one in doubt. In my opinion the first important disease to exclude is tuberculosis, because if the effusion is due to this condition an early treatment will be followed in the majority of cases by a functional joint, while treatment delayed until the joint is more or less destroyed must be followed by an excision. The possibility of a loose or dislocated cartilage must be thought of, especially when the joint affected is the knee. In making your prognosis you must not forget that the joint effusion may be the first symptom of a grave arthropathy, which will later, even in spite of treatment, go on to complete destruction of the joint, such as is associated with chronic rheumatoid arthritis, tabes dorsalis, or syringomyelia. The only case in my own observation in which I have thought the diagnosis of hydrops articulorum intermittens was justifiable was one I saw recently in consultation with Dr. F. R. Smith, of Baltimore. The patient was a woman, aged twenty-seven years, who had been married four years; no children. Following slight trauma, two years ago, over the anterior surface of the left tibia two ulcers formed, but healed slowly. A year ago she had a slight trauma to the left elbow. Following it was slightly swollen, since which time she has had remittent attacks of the same swelling of the elbow-joint. The periods have been pretty regular. The swelling is sometimes associated with slight pain and restriction of motion and the feeling of tingling and numbness in the fingers. On one occasion during a recent attack, without trauma, the other elbow was similarly affected. I saw her at the end of an attack, and there was an area of œdema, confined more to the subcutaneous tissues than to the skin, over the external condyle of the humerus. There was little effusion in the elbow-joint. Skin was normal. Fearing that perhaps there might be beginning new growth of some kind, although from the history and the careful examination I felt this could almost be excluded, I advised an exploratory operation. A few days before the operation most of the œdema disappeared. At the operation all the tissues were normal except the periosteum. In stripping this from the bone the outer table of the humerus seemed a little rougher than usual. Chiselling into the external condyle, the bone was normal. The wound healed kindly. Following the operation the œdema disappeared in a few days. About three weeks later, without apparent cause, she suddenly had the same swelling of the elbow, associated with a similar one, but to a slighter degree, of the opposite elbow, and a definite

area of œdema on the dorsum of the hand between the thumb and index finger. It disappeared after four days. She has now been free from an attack for three months. Here we have, therefore, history of a localized acute œdema, most marked in the left elbow-joint, involving the periarticular tissues, associated with slight effusion, recurring at irregular intervals, and on two occasions associated with a similar condition of the opposite elbow and skin of the dorsum of the hand. The patient was otherwise healthy, but of a marked nervous temperament and very hysterical. In this case the operation and the histological examination of the tissues demonstrated no pathological change. Previous prolonged treatment with mercury and iodides practically exclude lues. I must confess that until I read Schlesinger's article I was at a loss to explain the condition.

### TUBERCULOSIS OF BONES AND JOINTS.

On this subject I will refer chiefly to Krause.<sup>1</sup> Early diagnosis followed by proper treatment is practically impossible in tuberculosis of bones and joints without a very concise and extended knowledge of the pathological conditions. In the following review I will devote the space chiefly to pathology, and will leave to *PROGRESSIVE MEDICINE* for December, 1901, the more detailed discussion of the modern treatment (both conservative and operative) of tuberculosis of bones and joints.

The pathology of the tuberculous process in bone and synovial membrane differs only a little from that of other tissues. In the synovial membrane the gross and microscopical picture is modified by the excessive exudate common to synovial membranes. In the bone the picture is modified by the peculiar changes in the bony structure about the tubercle. Both have the tendency to caseation and liquefaction, with the formation of a cold abscess, which later may result in fistula.

**Tuberculosis of the Synovial Membrane.** Clinically, it is of much importance to recognize whether the synovitis is a primary or a secondary one. The gross and microscopical picture of the synovial tuberculosis does not differ, whether it is a primary or a secondary infection. When the primary disease is in the bone the joint may be infected by a perforation through the cartilage or into the sac of the capsular ligament, which in some joints extends beyond the border of the articular cartilage. In such instances the fistula between the bone focus and the synovial sac can be demonstrated.

If previous to the secondary infection of the synovial sac there have been no pre-tubercular irritative changes the direct infection of the

<sup>1</sup> *Deutsche Chirurgie*, Part 28a, Stuttgart, 1899.

healthy joint from the bone focus is associated clinically with very acute joint symptoms, marked swelling due to effusion, intense pain, and in some instances so great as to simulate acute pyogenic arthritis. In many instances the bone focus has given little, if any, clinical signs, and the onset of the trouble are the signs of arthritis, which is frequently associated with trauma. In some instances the distention of the joint is so great, especially in the hip, that pathological dislocation takes place. This, however, is rare, although the limb, especially when the trouble is at the hip, may take the position of a pathological dislocation. This acute arthritis with effusion soon subsides, and is followed by the ordinary clinical symptoms of bone and joint tuberculosis.

**Pre-tubercular or Irritative Synovitis.** Krause describes carefully the changes which may take place in a joint whose epiphysis is the seat of a tubercular infection. These irritative changes are more marked the larger the bone focus and the nearer its position is to the joint capsule, and also the presence of tubercular suppuration; the symptoms are always aggravated by trauma. Clinically the symptoms of the synovitis may predominate and the signs of tubercular osteomyelitis may be overlooked.

To open and examine such a joint, although we would find the evidence of an exudative synovitis, yet the microscopical study of the exudate or the synovial membrane would show no evidence of tuberculosis nor the presence of the tubercle bacilli, nor would a piece of tissue inoculated into an animal produce tuberculosis. For this reason we must constantly bear this possibility in mind in exploratory arthrotomy. This irritative synovitis may consist simply of an exudate, and clinically gives the ordinary symptoms due to effusion. As a rule, the effusion is transitory. It may be remittent; therefore, a sudden effusion in any joint, especially when we can ascertain a previous history of pain and bone tenderness, points to tuberculosis of one of the epiphyses. In other cases there is more serious change in the synovial membrane; we find that it is congested and distinctly thickened; its surface, instead of being smooth, is granular and hyperæmic. Dilatation of the vessels is more marked along the border of the articular cartilage, where there may form distinct villi growing over the cartilage. Many surgeons are in the habit of calling such a picture tubercular synovitis. The irritative synovitis may even be more extensive, and the gross appearance is very much like that seen in the arthritis associated with pyogenic osteomyelitis, and this synovitis is more common in the latter condition. Volkmann has described it as "pannosen chondritis or synovitis." In this condition the dilated vessels at the cartilage border are more marked and overlap the cartilage to a greater extent, with a production of marked villi. There is with this a distinct destruction of the synovial

membrane ; the synovial cavity may become obliterated at one or many places, with finally complete obliteration ; there may be with this erosion of the cartilage and ankylosis. Nevertheless, with these extensive changes we do not find the tubercle bacilli, nor in pyogenic osteomyelitis the pyogenic cocci. This destruction of the synovial membrane, and especially the erosion of the cartilage, favors perforation from the tubercular focus in the bone. However, when such changes have taken place in the joint, and the synovial membrane is partly or completely obliterated, perforation of the bone focus does not produce clinically the same marked symptoms of arthritis as in those instances in which the joint is healthy, so that in the majority of cases we cannot recognize clinically when this extensive pre-tubercular destructive synovitis becomes infected with the tubercle bacilli. In tuberculosis of the bones about the shoulder or knee-joint the synovial sac is generally obliterated before perforation takes place, so that in these joints the onset of acute arthritis is rare. In the hip, on the contrary, perforation early into the normal synovial sac is not uncommon, and the history of an acute arthritis in the early days of tuberculosis of the hip is of a more frequent occurrence.

**Tubercular Synovitis.** The involvement of the synovial membrane in acute general miliary tuberculosis is of no surgical importance. There are two chief forms of tuberculosis of the synovial membrane, whether it is primary or secondary. The first, that described by König as *parenchymatous synovitis*, consists chiefly in a granular thickening of the synovial membrane, frequently to 1 cm. or more, and is accompanied with little or no exudate, either serous or purulent. The gross appearance of this granular form of synovitis is quite characteristic ; there is a distinct exudate in which we plainly see tubercles. There is seldom caseation or liquefaction necrosis, except now and then as a pin-point in the centre of a large tubercle, which has either a white or a yellow centre. This granular synovial membrane is firmly fixed to the surrounding tissue, and does not peel away like the ordinary extra-articular tubercular abscess. We usually can recognize at least three layers in the thickened synovial membrane. The inner layer, consisting chiefly of the organized exudate, is anæmic ; the middle layer, which is the altered synovial membrane itself, is very vascular. In these two layers we find scattered tubercles. The outer layer consists of very dense fibrous tissue in which there are seldom, if ever, tubercles. One can separate the first two layers from the third very easily, but the first and second layers are firmly adherent, similar to the adhesions of the third layer to the extra-synovial tissue. In the second form of tubercular synovitis the tendency to caseation and liquefaction necrosis is very marked ; there is an excessive joint effusion and the formation of all forms of joint bodies.

In addition, perforation, as a rule, takes place early, with a formation of extra-articular abscesses.

The tendency in the first form is toward slow healing, with ankylosis, frequently associated with joint contractions; in the second form to extra-articular abscesses and fistula, with extensive infiltration of the soft parts about the joint. Rarely the second form is secondary to the first.

**JOINT CONTENTS AND BODIES IN TUBERCULAR SYNOVITIS.** The exudate may be serous or fibrous. Now and then we find red blood-cells, but the effusion is rarely hemorrhagic. The rice bodies (*corpora oryzoidea*) are formed from the exudate, and are seldom found except in a joint in which there is some motion. The size and shape are due to the moulding in the movable joint. Tubercles and tubercle bacilli have been demonstrated in these rice bodies. The exudate may be pure pus, and we then have a cold-joint abscess. This condition is more frequent in primary synovial tuberculosis.

There is a third and less common variety of tubercular synovitis—the *knotty form*. Here we see usually a solitary large, circumscribed tubercle; it may even be the size of an egg, generally flattened, due to pressure, and it may be pedunculated. The knotty form occurs in two varieties; in one it is fibrous, of a jelly-like consistency, of grayish-red color, and of large size; surrounding it there may be a few miliary tubercles. In the other variety the tubercle is inclined to caseation and suppuration.

**Lipoma Aborescens Tuberculosum.** Although rare, the tubercular synovitis may be associated with hypertrophy of the villi of the synovial membrane. The increase in the size is due chiefly to fat. The tubercular infection may be primary or secondary. The masses of fat are of all sizes and take various shapes. In many one can recognize the tubercles with the naked eye. (See Figs. 58 and 59.)

**Hydrops Tuberculosis.**<sup>1</sup> In connection with the pathological and clinical study of tuberculosis of the synovial membrane it is of interest to study that clinical form in which the chief symptom is joint effusion, and which has been designated by König as hydrops tuberculosis. In a typical case of hydrops the effusion is the predominant symptom, while the thickening of the synovial membrane and periarticular tissue is very slight or not present at all. For this reason in the early period of the disease the diagnosis is difficult. This condition is usually associated with primary tubercular synovitis, and rarely the onset of the effusion is an acute one, when we have the clinical picture of acute synovitis with effusion. In the majority of instances the effusion forms

<sup>1</sup> Krause, *Deutsche Chirurgie*, p. 137.

painlessly and without acute, general, or local symptoms. The effusion may attack one or a number of joints; the hydrops may be remittent.

FIG. 58.



Four-fifths natural size.

FIG. 59.



Natural size.

FIGS. 58, 59.—Secondary tuberculosis of exceedingly hypertrophic joint-villi, from the right knee-joint of a strong and otherwise healthy man, aged twenty-three. Tubercles plainly visible, natural size (Fig. 59). The man suffered for years with pain in the joint. After excision of tumors, healing; flexion possible to right angle. (From KRAUSE.)

If one joint is attacked, the effusion after aspiration, or without it, may disappear, and there may be no further symptoms; or it may extend



gradually into the picture of chronic tuberculosis of the joint. When a number of joints are affected all but one may recover, while this one assumes the picture of chronic tuberculosis. With the first appearance of the effusion there may be no symptoms except slight fatigue of the limbs; now and then there may be slight restriction of motion. If the effusion is excessive and not treated the joint capsule becomes over-stretched, and we get a relaxation of the joint similar to the arthropathies in syringomyelia and tabes.

The formation of loose bodies in the joint is common in hydrops. The diagnosis can usually be made by aspiration, especially if one has the good fortune to withdraw a loose piece of synovial membrane. The microscopical study of this tissue will demonstrate the tubercle. Arthrotomy, with inspection of the joint, will always confirm the diagnosis. Hydrops tuberculosis, especially if due to primary synovitis, gives the best results from aspiration and iodoform injections, or, better, arthrotomy with irrigation of the joint, followed by iodoform injections.

Clinically, the most important facts to be borne in mind are that now and then tuberculosis may begin as a polyarticular disease, with effusion. One joint later assumes the ordinary picture of chronic tuberculosis; also the infection may begin as an acute arthritis, with effusion; but, as stated before, this is more frequently associated with perforation of the normal joint from a bone focus, but may be the onset of a primary tubercular synovitis.

**Tuberculosis of the Bone.** In *PROGRESSIVE MEDICINE* for December, 1899, Nichols' observations were quoted, in which from examination of over 120 tubercular joints he was unable to positively demonstrate a case of primary tubercular synovitis. The observations of Krause, König and others from a much larger experience demonstrate that primary tubercular synovitis is possible, although less frequent than secondary synovitis from bone tuberculosis. For this reason, in every instance in which from clinical signs tuberculosis of the joint is suspected, the greater possibility of bone involvement must be borne in mind.

**SITUATION OF THE BONE FOCUS.** Tubercular osteomyelitis in the great majority of cases is localized in the epiphysis of the long bone; it may, but not very commonly, secondarily infect the medullary cavity of the diaphysis. The opposite is true of pyogenic osteomyelitis; here the pyogenic cocci are generally localized in the diaphysis, near the epiphyseal line, and usually extends in the direction of the diaphysis, and less commonly into the epiphysis. The older the individual the less frequently is the epiphysis the seat of a pyogenic osteomyelitis. The possibility of primary tubercular osteomyelitis of the diaphysis has already been discussed.<sup>1</sup> Krause's observations confirm those of Kütt-

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1899, p. 193.

ner and others there quoted. Fig. 60 is an excellent X-ray photograph ; it shows a tubercular abscess in the diaphysis of the tibia in a girl, aged eleven years. It should be compared with that of Küttner.<sup>1</sup> Fig. 61 is an excellent X-ray photograph of the same case four days after chiselling, and demonstrates the definite localization of the disease of the diaphysis. Fig. 62 is an X-ray photograph of the same case five months later, and demonstrates the organization of the blood-clot and the filling up of the cavity with new bone.

FIG. 60.



Tuberculous abscess in diaphysis of tibia in a girl, aged eleven years. Half natural size.  
(From KRAUSE.)

**Tuberculosis of the Diaphysis of the Short Pipe Bones.** (*Spina Ventosa*.) This is much more common, but as its clinical recognition is much easier, and the indications for operative treatment much simpler than the tuberculosis of the epiphysis, we will not use space for its con-

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1899, p. 195.

sideration, but will simply reproduce two excellent X-ray photographs from Krause, which show beautifully the shadow of the bone destroyed by osteomyelitis. (Figs. 63 and 64.)

**Tubercular Osteomyelitis of the Epiphyses of the Long Pipe Bones.** Surgeons who desire to be able to diagnose tuberculosis from its gross appearance must school themselves in the normal appearance of the bone at the different periods of life and the changes due to the

FIG. 61.



FIG. 62.

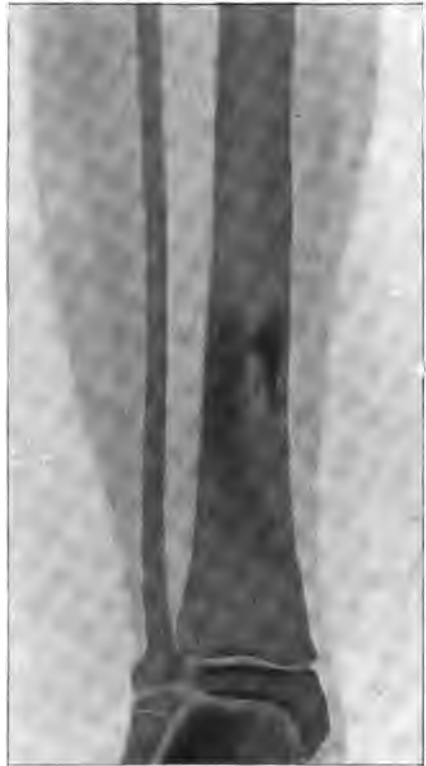


FIG. 61.—Same as Fig. 60. Four days after chiselling, immediately preceding secondary suture. Half natural size. (From KRAUSE.)

FIG. 62.—Same as Fig. 61. Five months later. (From KRAUSE.)

disease. This can be accomplished only by the most careful scrutiny of the naked-eye appearance of the tissues at operation and much less frequently at autopsies. One should be able in the majority of cases, from the naked-eye appearance, to differentiate syphilitic, tubercular, and pyogenic osteomyelitis, sarcoma, lipomasia, and metastatic carcinoma of the bone. On such differentiation the character of the operation and the extent of the removal of the diseased bone depends. In children,

on account of the normal presence of red marrow, the localization of the tubercle is never so well defined as in the adult. In the adult the hemorrhagic area about the tubercle stands out clearly from the normal yellow marrow. The tubercle may be situated in any part of the spongiosa of the epiphysis. It is usually single, although there may be multiple fossi. As a rule, but one bone of the joint is involved, yet there may be single or multiple fossi in the ends of both bones.

FIG. 63.



Spina ventosa at base of phalanx on the left large toe in a boy, aged eleven years. Four fifths of X-ray. Destruction of bone by tuberculous granulations. Six months later the entire base of phalanx was found destroyed to the base. (From KRAUSE.)

We seldom see the tubercle in its early stages, but one should be able to recognize its appearance. In the spongiosa one should see a well-defined, translucent, grayish-red or yellowish-white or yellow area. In the adult there is a distinct hemorrhagic rim.

**THE GROSS APPEARANCE OF THE DISEASE.** The bone lamellæ are softened or absent. If the process is an acute one the meshes of the

FIG. 64.

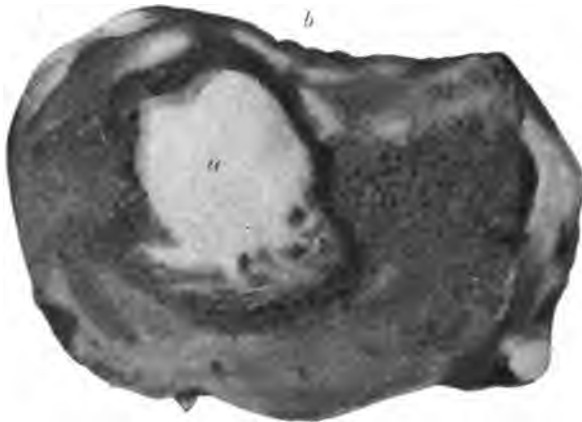


Tuberculosis of metacarpal bone. Three-fourths natural size. (From KRAUSE.)

cancellous bone about the tubercle are widened and the marrow spaces are filled with hemorrhagic marrow. If the process is a chronic one the hemorrhagic zone is less and the cancellous bone is sclerotic. At this stage complete healing may take place; the tubercle is converted into

scar-tissue, surrounded by an area of eburnated bone, or the tubercle may remain intact and become encysted by a fibrous membrane surrounded by sclerotic bone. In the latter instance of apparent healing, relapse, with further infiltration of the tubercular process, may take place, even after many years, and is always associated with some trauma. This should always be borne in mind, that apparently healed bone tuberculosis may relapse at any time. This fact is the chief contraindication of a forcible correction of any deformity in apparently healed tubercular osteoarthritis. In other instances the tubercular focus increases in size and the granulation tissues destroy by bone absorption the cancellous bone; but in the area about the disease, in addition to osteoporosis, there is always more or less osteosclerosis. In the more

FIG. 65.



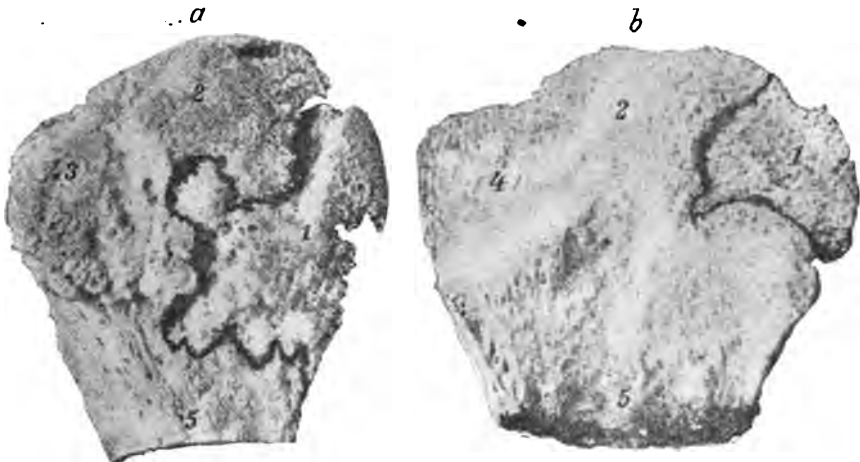
Grave tuberculous arthritis of the knee in a man, aged forty-four years. Resection of knee-joint. Lower surface of sawed-off piece of tibia. Natural size. Unusually large caseous sequester (*a*) completely separated from surroundings. Bone-cavity dressed with abscess membrane (*b*). This cavity had penetrated into the joint by means of a fistula. (From KRAUSE.)

acute form there may be extensive infiltration by the tubercular granulation tissue of the marrow spaces, which gives to the spongy bone a mottled, reddish, and characteristic grayish appearance. The presence of the grayish granulation tissue in the marrow spaces, with here and there a hemorrhagic space, with slight widening of the marrow cavities, is a positive evidence of the infiltration of the tubercular osteomyelitis beyond the original focus. As a rule, this extends toward the periosteum or toward the bone cartilage, seldom in the direction of the diaphysis.

**FURTHER PROGRESS OF THE BONE FOCUS.** The area of tubercular osteomyelitis may undergo caseation. If the lamellæ are preserved we get a caseous sequestrum, as shown in Fig. 65. It may undergo liquefaction, when we get a bone abscess, which, as a rule, is surrounded by

a definite membrane composed of an inner lining, which consists chiefly of tubercles and granulation tissue and an outer fibrous lining. This abscess membrane is easily peeled from the surrounding bone. It is very common in tuberculosis of the epiphysis to see a formation of small wedge-shaped sequestra, shown in Fig. 66. These tubercular, wedge-shaped sequestra can, as a rule, be easily distinguished from pyogenic sequestra, as they generally involve a part of the epiphysis, although in some instances they may extend to the diaphysis (Fig. 67). In addition the sequestra may be entirely or partly caseated, or in the marrow cavities of the cancellous bone we can recognize the characteristic grayish tubercular granulation tissue.

FIG. 66.



Tuberculosis of right shoulder-joint. Resected head of bone. Natural size. *a*. Photographed from front: 1. Very large, completely separated sequester. 2. Head deprived of cartilage and carious. 3. Greater tuberosity. 5. Diaphysis. *b*. Preparation sawed through the frontal plane: 1. The sequester reaching the joint, surface deprived of cartilage is wedge-shaped. 2. Extensive caseous infiltration of the head; secondary infection from sequester in greater tuberosity (4), and the diaphysis (5). (From KRAUSE).

**Involvement of the Bone and Cartilage.** The irritative synovitis associated with tubercular osteomyelitis of the epiphysis has already been described. The tubercular focus in its growth may directly perforate through the joint cartilage into the joint and produce at once a tubercular synovitis; or as it nears the cartilage border the change in the cancellous bone interferes with the circulation of the cartilage, and the cartilage becomes loosened, either in small areas or in some instances the entire articular cartilage may become separated. This partial or complete separation of the joint cartilage is almost pathognomonic of tuberculosis, and the surface of the bone beneath the marrow cavities is filled with characteristic gray granulation tissue, which, in addition,

has a mottled, hemorrhagic appearance. The bone is usually soft, and can be easily cut with a knife.

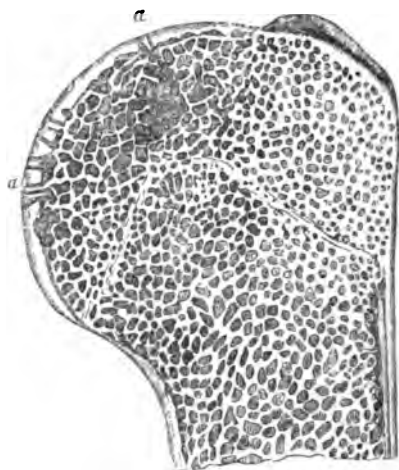
The extension through the cartilage may take place by multiple minute perforations, as shown in Fig. 68.

FIG. 67.



Lower end of tibia, sawed through almost frontally. Large and completely separated caseous sequestrum situated in a cavity in the tibia. At *a* the perforation to outward has taken place. Three-quarters natural size. (From KRAUSE.)

FIG. 68.



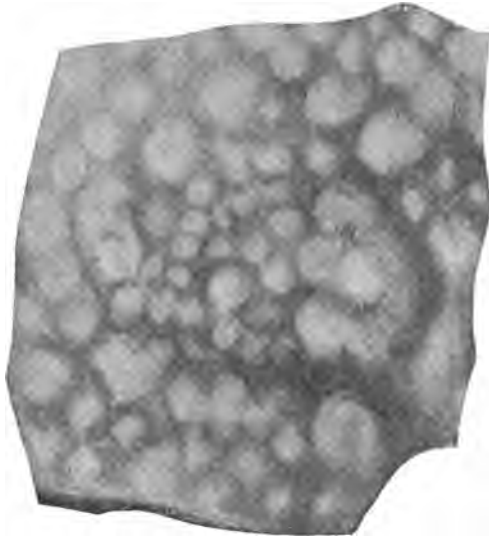
Beginning fungous inflammation of the shoulder-joint in man who died at age of twenty-one years from purulent coxitis. Saw cut through the head of the humerus. Origin of trouble from bone. The part of the epiphysis turned toward the joint cartilage, rarefied, marrow spaces filled with dark-red granulations, which have already completely destroyed the lamellæ of compact bone substance beneath the cartilage and have partly begun to eat into the cartilage at its lower surface, partly have perforated it like a sieve. *a a*. Joint-capsule perforated like a sieve. (From KRAUSE.)

**Periostitis and Extra-articular Abscess.** When tuberculosis of the epiphysis extends toward the periosteum we get at once a periostitis. In many instances from irritation there is a distinct non-tubercular periostitis, recognized clinically by increased bone tenderness, thickening, and roughening, recognized by the gross appearance of new periosteal bone. When this becomes infected with the tubercle bacillus we may have caseation or a suppuration beneath the periosteum; more frequently, however, the periosteum itself is perforated, and we get the characteristic extra-articular cold abscess. This abscess is always lined by a definite membrane, having the peculiar characteristic that it can be



easily peeled from the surrounding tissues. As a rule, this inner surface has the characteristic appearance of tubercular granulation tissue, as seen in Fig. 69. This abscess may rupture and form a fistula.

FIG. 69.



Abscess membrane from tuberculous abscess resembling frog-roë. Surface aspect slightly magnified. (From KRAUSE.)

**Lipomasia.** The softened condition of the bone designated by this term should be recognized and not be mistaken for a disease. Lipomasia is a condition of the cancellous bone in which the spaces are widened and filled with fatty marrow, which, as a rule, is very anæmic. This bone is soft and brittle. It fractures and cuts easily. It is present not only in tuberculosis, but in any condition in which the limb has for a long time been at rest. It is also a senile change. Bone in this condition should never be removed; it heals well, and later when the limb is used again it becomes converted into the normal cancellous bone. Krause states that many inexperienced surgeons have mistaken this fatty cancellous bone for disease, especially tuberculous, and for this reason have removed it, thereby making the resection a much more extensive operation, with the result of deformity.

**Changes in the Periarticular Tissue about the Tubercular Joint.** Everyone is familiar with the characteristic boggy appearance and feeling of the periarticular tissues in tuberculosis, which undoubtedly gave rise to the term *tumor albus*, or white swelling. This infiltration or new formation in the periarticular tissue is due in some part to the irritation of the infection and in some part to restricted circulation. It

varies in its consistency ; for example, the periarticular infiltration may be very sclerotic, and in such instances the thickening is not great, and the term *tumor albus fibrosa* has been used for this condition. In the second form the tissues are soft and vascular, the thickening is irregular, and there may be pseudofluctuation, and this has been called *fungus articuli*. In a more marked manner the tissues may be almost gelatinous. In such instances there is extensive serous infiltration, designated by English surgeons as gelatinous infiltration or degeneration, and by Virchow as "myxomgewebe." In these changed periarticular soft parts tubercular infiltration is not necessarily present. This periarticular thickening or bogginess which obliterates the normal depression about the joint is almost pathognomonic of advanced tuberculosis of the bone and synovial membrane.

**The End Results of Bone and Joint Tuberculosis.** The possibility of complete healing of small tubercles in the bone or of the primary synovitis, with slight effusion, has already been discussed ; also the possibility of apparent healing in which the tubercle is only encapsulated, and which at any future time may be easily ignited again into an acute process by a slight trauma. Both tuberculosis of the bone and synovial membrane may proceed to a more advanced stage, yet healing takes place at this period, with complete restoration of the function of the joint. This is, however, rare ; as a rule, there is some restriction of motion in the joint, due either to the destructive changes of the tuberculous process itself on the synovial membrane or cartilage or to the changes already described in irritative synovitis ; so that in the majority of cases more or less, and sometimes complete, ankylosis is the end result. If the limb heals in a position of contraction we have to bear in mind the changes of growth in youthful individuals at the joint ends, due to changes in pressure, and, more important, we must bear in mind the possibility of atrophy or some form of deformity due to partial or complete destruction of the epiphysis by the tubercular process. As a rule, in tuberculosis the entire epiphysis is seldom destroyed, and one is more apt to get a partial destruction with an increase of growth of the unaffected part, producing different forms of lateral deformities, as genu valgum and varus. Not infrequently, instead of atrophy there is distinct increase of growth in the long bones, caused by the continuous irritation of the tubercular osteomyelitis, seen chiefly in very chronic cases with small foci. It is not uncommon to notice when we have tuberculosis in the young of long duration that the entire limb and the foot are smaller than the opposite. The enforced rest necessitated by the disease unquestionably is the cause of the retarded growth of the other bones. The condition of fat-atrophy or lipomasia of the bone near the disease, or of the entire limb, have already been described.

**DIAGNOSIS.** No matter whether the surgeon follows the operative or conservative treatment, he wishes to make a diagnosis as early as possible in this disease, because the results correspond in almost a direct relation to the stage at which the treatment was begun. The advanced clinical picture of the joint tuberculosis is pathognomonic and can be seldom mistaken. The diagnosis in the earlier stages is more difficult. Clinically, muscle spasm, with a tendency to contraction, associated with atrophy of the muscles above and below the joint, is suggestive. Bone pains and areas of bone tenderness at the epiphysis point to tubercular osteomyelitis. The beginning characteristic periarticular boggiess of those joints not situated too deeply is a very important diagnostic sign. The X-ray photograph, as a rule, does not picture any but large foci of bone tuberculosis; but in the hip it will show changes in the head and neck, due to pressure, which are practically only present in tuberculosis. The tubercular infection of the synovial membrane is best diagnosed by exploratory arthrotomy, which can be performed under cocaine. In many cases simple inspection of the synovial membrane is sufficient for a positive diagnosis. The histological study of a piece of tissue and the inoculation of a second piece into an animal are positive methods. However, we must remember that if we find no histological evidence of tuberculosis in the diseased synovial membrane, this does not exclude the possibility of an irritative synovitis associated with a tubercular osteomyelitis in one of the epiphyses; so that it would appear that an exploratory chiselling into the bone would be the only positive method of diagnosis in the early stages. Krause does not suggest this.

**TREATMENT.** *Tuberculin Reaction.* Krause condemns the use of Koch's tuberculin for diagnostic purposes. For a number of years in Professor Halsted's clinic in the Johns Hopkins Hospital we have used a tuberculin obtained through the courtesy of Dr. Trudeau. We have found this tuberculin absolutely harmless except in advanced cases of tuberculosis, where it is not needed. Its diagnostic value has been of the greatest importance, and in *PROGRESSIVE MEDICINE* for 1901 our own observations and those of others in the literature will be carefully described.

Krause is inclined, with a great majority of surgeons, to the conservative treatment of tuberculosis of bones and joints, under similar rules to those described in tuberculosis of the hip. His experience and that which he has collected from the literature point to the good results from iodoform injections. The early operative treatment as compared with the conservative arthrotic treatment will be discussed in *PROGRESSIVE MEDICINE* for 1901.

### TUBERCULOSIS OF THE HIP.

The new observations and work on coxa vara, or curvature of the neck of the femur from its various causes, as classified by Alsberg, and especially coxa vara traumatica of Sprengel, have contributed much to our knowledge in the differential diagnosis of conditions at the hip-joint and upper end of the femur. All authorities agree that many cases heretofore treated as tuberculosis of the hip have without much doubt been some form of coxa vara. It is a question whether or not many of the favorable results recorded for the conservative treatment of tuberculosis of the hip do not belong rather to coxa vara.

**Conservative Orthopedic Treatment versus Excision for Tuberculosis of the Hip.** In recent years the majority both of orthopedic and general surgeons favor the non-operative or conservative management of tuberculosis of the hip, and although much has been written on this subject, nevertheless a recent article from Hoffa's clinic in Würzburg, by Romanus Binder,<sup>1</sup> is most welcome. In a short but very clear article Binder gives us a brief *résumé* of the history, collects the most important and careful statistics, and most conscientiously compares the orthopedic treatment with the operative treatment, consisting of excision. In addition, he reports twenty-two cases which were treated in the private clinic of Professor Hoffa with the best and most approved orthopedic apparatus. With the introduction of antiseptic surgery, and for some time after, the operative treatment, which consisted of both early and late excision, was given a fair trial by surgeons almost the world over. Later, the orthopedic surgeons began treatment with more improved apparatus, so that after a few years we were able to compare excision with better technique, with conservative treatment, with better apparatus. The result has been to change the method of treatment from the operative to the non-operative.

*The Mortality.* Considering the great number of figures in numerous large clinics, the mortality of operative and non-operative treatment of tuberculosis of the hip is about the same—from 40 to 50 per cent. This mortality considers not only the recent but the more remote causes of death, the cases being followed for a number of years. In 88 per cent. of the cases the cause of death is tuberculosis, either local or general. Other causes were pyogenic infections of the joint or its surroundings, amyloid degeneration, or exhaustion from prolonged suppuration.

As to the ultimate results, statistics show that on the whole in the non-operative orthopedic treatment there is less atrophy of the leg, less shortening, but more cases of contraction; while after excision, although contraction is less common, this result is detracted from by the number

<sup>1</sup> Zeit. f. Orthopädische Chir., 1899, Band vii., Heft 2 and 3, p. 276.

of cases of frail joints. This comparison, however, between the operative and non-operative treatment of tuberculosis of the joint considers those cases of tuberculosis of the hip in which a complete excision of the head, sometimes even the neck and trochanter, has been done. Unquestionably, a complete excision, if done sufficiently early and not in too advanced disease, removes the local disease, but there will always be a greater degree of shortening, and unless the remainder of the shaft is placed in the acetabular cavity there will be a frail joint. Unquestionably, if excision is the rule in every case much bone will be removed which without operation would have been restored to its normal condition. These statistics unquestionably demonstrate that the excision of the joint is not the operation of choice, but simply the operation of necessity in certain cases in which the tubercular osteomyelitis has practically at the time of operation destroyed the head and neck of the bone.

**ORTHOPEDIC TREATMENT.** Binder gives two cardinal rules: (1) Absolute fixation of the joint and extension. This should not be done by the older method of Volkmann, in which the patient is kept in bed for many months or years, but by an apparatus which fixes the joint and produces at the same time extension, and which will allow the patient to get up and about on crutches. The introduction of this ambulatory treatment of tuberculosis of the hip is unquestionably one of the most important advances in orthopedic treatment. (2) In addition to this the open-air treatment, now used in all forms of tuberculosis, must not be neglected. When in the older method the patient was kept in bed, the difficulties surrounding the transportation of the bed into the open air were sufficient to make it impracticable in the majority of hospitals or at home; but if the patient is able to be up and about in his ambulatory apparatus, the open-air treatment becomes a simple matter.

*Iodoform Injection of the Joint.* According to Binder (Krause also) this is an important adjunct to the orthopedic apparatus, and should be practised in the majority of cases.

*Plaster-of-Paris Dressing.* Binder, in the out-patient department among the poor, believes that this is sufficient. There are a few points in the method in which he applies the plaster which are important ones for the general practitioner in this country to know. The leg, if possible, should be put up in slight flexion and abduction. Flexion allows the patient to sit down more easily, and abduction is the position that we wish the leg to be in at the end of the cure if there should be ankylosis. The plaster should not only take in the affected leg from the sole of the foot including the hip, but should extend to the nipple line. This high extension of the plaster cast to the nipple line is a procedure much neglected in this country. It is one which I have always followed in every dressing in which I attempt to fix absolutely the hip-joint. In addition to this, Binder recommends that the opposite non-affected hip should be

included in a plaster cast down to the knee, so that the pelvis of the patient is absolutely fixed. As an additional support in the early days of treatment, a splint should extend between the cast slightly above the level of the two knees. This unquestionably is the only form of absolute fixation in plaster. So far as my experience goes, I have never found it necessary to fix in plaster the opposite thigh; yet perhaps in those cases which we have kept in bed on extension, because the routine plaster cast was painful, this additional fixation, by including the other thigh, would have allowed us to use the ambulatory treatment earlier. As Binder says, in his experience this plaster treatment, if properly followed, gives as equally good results as when the ambulatory treatment has been followed with some form of splint. A number of different splints are recommended; the object of all is complete fixation with some extension in the slightly fixed and abducted position, the patient walking with crutches on a high-heeled shoe on the unaffected leg. In twenty-two cases reported from the private clinic of Professor Hoffa the treatment throughout was with Hessing's apparatus, which has been described by Hoffa in his most recent text-book. In addition to this there has been massage with soft-soap (*Schmierscife*). In four of the twenty-two cases from Hoffa's clinic there were almost perfect results. In six cases, including these four, the position was an excellent one. In six further cases position of fixation was in a medial position. In eight cases there was slight flexion; in five of these associated with slight *adduction*; in one with a slight *abduction*; in two with outward rotation, and in one case there was full extension with *adduction*. In not a single case was there a great degree of contraction, although a number of the cases were quite grave when they came for treatment. In every case there was shortening. The ultimate results, therefore, in these twenty-two cases, although small, represent the possibilities of the orthopedic treatment when carried on under the most improved plans in patients who could afford the best apparatus and the best attention, which undoubtedly was combined with the best method of climatic treatment. If abscesses form Binder advises their incision, and if there are sinuses the treatment with curettage in addition to the iodoform injection of the joint. The operative treatment is reserved only for cases of complete ankylosis in marked positions of contracture. The operations consist of osteotomy or the cutting of the soft parts. The forcible correction of the deformity under anæsthesia at one treatment is condemned, agreeing with the majority of authors (see Krause). Binder states that if the ankylosis is complete when first seen one cannot hope from any form of orthopedic treatment to correct the position; but in those cases in which there is some motion between the femur and the pelvis much can be done by persistent and gradual correction with orthopedic apparatus.

**The Modern Orthopedic Treatment of Tuberculosis of the Hip.**

According to Binder, the following is a summary of the proper treatment. The moment the diagnosis is made treatment should begin. The earlier treatment is begun, naturally the better the results. Even with the very slightest symptoms, such as muscle spasm, slight pain, etc., the most conscientious, even prolonged, treatment should be followed. In early cases the plaster dressing or the apparatus which produces fixation and extension can be put on at once. In more advanced cases in which the muscle spasm is more intense and in which the contracture positions are more marked the apparatus may not be suitable for some time. Such cases will probably have to have extension in bed for a few weeks and then successive plaster casts, and after the contraction position is somewhat corrected and the muscle spasm has somewhat disappeared the apparatus is applied. The apparatus or the plaster cast is continued until all pain in the hip has disappeared—until attempts at motion at the hip and concussion on the trochanter and on the sole of the foot do not produce pain. After all the symptoms of local pain and tenderness have disappeared for a number of weeks, during which time the patient has not been allowed to place the affected leg to the ground, the cast or the apparatus may be discontinued; but for a number of months the patients should be compelled to wear a protection to the hip, which consists of leather or some form of felt. This should be continued even after the crutches have been thrown away. The average orthopedic treatment, even in a case seen early, requires from two to four years. In the early period of the disease iodoform injections should be practised. If abscesses form they should be incised. If the ankylosis is complete and in a position of contracture, later osteotomy and tenotomy should be done to correct the position, but not until the evidence of local healing has taken place. During all this time the patient should be kept out in the fresh air as much as possible.

**Early Exploratory Operations in Tuberculosis of the Hip.** Bloodgood<sup>1</sup> takes exception to the routine non-operative and orthopedic treatment of tuberculosis of the hip. For many years (1893 to 1899) a treatment similar to that advocated by Binder had been practised in the clinic of Professor Halsted, of the Johns Hopkins Hospital. Although the results had been good, there seemed to be room for much improvement upon the usual orthopedic treatment. Bloodgood had in mind for some years early exploratory operations in which the surgeon might be fortunate in finding the focus of disease in the bone at a period when its complete excision, or, if the tubercular osteomyelitis was more extensive, a partial excision might be done without interfering with the con-

<sup>1</sup> Johns Hopkins Hospital Bulletin, January, 1900.

tinuity of the bone or the function of the joint. His first object in the early operation for tuberculosis of the hip was to avoid a complete removal of the head or any amount of bone sufficient to interfere with the continuity of the upper end of the femur or the function of the joint; to excise the diseased bone only in small areas by the gouge and curette, trusting to antiseptic irrigations, iodoform, and especially to the healing process to check the further extension of the tubercular process and to encourage healing of the disease, both of bone and soft parts. The more frequently one operates and the earlier in the disease the more frequently he may be fortunate in finding a single focus of tubercular osteomyelitis which can be completely excised without injury to the continuity of the upper end of the femur or the function of the joint, as shown in Cases I. and IX. of his reported cases.

Since writing this paper, in January, 1900, a further experience of eight months has confirmed these observations, and a longer following of the cases already operated on has demonstrated more and more the advantage of early operation. When orthopedic treatment is compared with an operation which consists in every instance of the complete excision of the head or more of the upper end of the femur, then, although the disease may be cured more rapidly in the operative cases, the functional result will always be bad, especially as to shortening, although if properly performed there is no reason to have the frail joints recorded by Binder. As Krause states, effusion into the joint is one of the earliest symptoms of tuberculosis, whether it is primary or secondary in the joint membrane. Sufficient experience has demonstrated that the arthrotony and irrigation with iodoform injection is the best treatment for the distended and inflamed capsule, whether the synovitis is as yet tubercular or not. In the non-operative cases, even under the most improved orthopedic treatment, according to Binder, there is always shortening. This demonstrates that there is some destruction either of the head of the bone or the acetabular cavity, allowing dislocation upward of the trochanter and shaft. It is not uncommon for the head of the bone to be entirely absorbed, or the neck absorbed so that the trochanter is in juxtaposition to what is left of the head. Early operations should either completely remove the focus of the disease in the bone, or, by the treatment just mentioned, prevent further destruction of the bone; and the shortening should be that which is present before operation. Extra-articular abscesses are not uncommon during the most improved orthopedic treatment. Early operation should prevent the formation of such abscesses. When abscesses are present the exploration of the joint and removal of the source of the disease in the upper end of the femur, in addition to the incision of the abscess or the curetting of the sinus, should be followed by more rapid healing.



# DISEASES OF THE KIDNEYS.

BY JOHN ROSE BRADFORD, M.D., F.R.C.P.

## ALBUMINURIA.

THERE are still many points of difficulty and doubt in the interpretation both of the pathology and the significance of the presence of albumin in the urine. There is a tendency for medical opinion to pass from one extreme to the other, in that formerly all cases presenting albuminuria were looked upon as serious, whereas now the mere presence of albumin in the urine is not usually held to throw very much light either on the nature or on the probable course of the condition giving rise to it, the diagnosis of the significance of albuminuria being made very largely on the associated symptoms presented by the patient. This renders the interpretation of cases presenting albuminuria without any other marked symptoms one of singular difficulty, inasmuch as it is clearly established that there are many conditions in which albumin, even in considerable quantities, may be present in the urine without entailing serious consequences; yet it is unquestionable that grave renal disease may sometimes exist, giving rise to few symptoms except the presence of albumin. It is, therefore, of the utmost importance to the practitioner to separate, if possible, the albuminuria of serious import from that which is due if not to trivial conditions, at any rate to conditions that do not seriously threaten life. Many attempts have been made in the past to differentiate the different varieties of functional albuminuria from those of organic disease, either on differences said to be presented by the albumin itself or else by other associated phenomena of the urine. It has been asserted, for instance, that in many cases of so-called functional albuminuria the composition of the proteid matter in the urine was different to that found in the albuminuria dependent on organic disease—in the one case both albumins and globulins being present; in the other only globulins. This distinction, like many others that have been raised, has not, however, stood the test of time, and it is generally recognized at the present time that no distinction can be drawn from conclusions based on the mere variety of proteid matter present; at any rate, with reference to the supposed significance of the presence of albumin with or without that of globulin. The presence of

tinuity of the bone or the function of the joint. His first object in the early operation for tuberculosis of the hip was to avoid a complete removal of the head or any amount of bone sufficient to interfere with the continuity of the upper end of the femur or the function of the joint; to excise the diseased bone only in small areas by the gouge and curette, trusting to antiseptic irrigations, iodoform, and especially to the healing process to check the further extension of the tubercular process and to encourage healing of the disease, both of bone and soft parts. The more frequently one operates and the earlier in the disease the more frequently he may be fortunate in finding a single focus of tubercular osteomyelitis which can be completely excised without injury to the continuity of the upper end of the femur or the function of the joint, as shown in Cases I. and IX. of his reported cases.

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casts in the urine was also at one time supposed to afford a criterion which would distinguish infallibly between functional and organic cases. In organic disease doubtless casts are present in greater abundance and in greater variety, and some casts are limited to organic disease; but some of the commoner casts are found also in cases of albuminuria of other origin, so that the presence in the urine of scattered hyaline casts is not conclusive evidence in effecting a diagnosis between functional and organic albuminuria. The quantity of albumin present is also most misleading, inasmuch as in some of the gravest renal diseases traces only of proteid matter are present, and in some varieties of functional albuminuria considerable quantities are present, although it is probable that it is rare for large quantities to be present in functional disease. A further difficulty is introduced in the interpretation of the significance of albuminuria, from the fact that not only may this condition be present in functional diseases and in organic diseases of the kidney, but small quantities of albumin are not uncommonly present as the result of the contamination of the urine by some albuminous secretion, and more especially, perhaps, from the persistence of a slight lesion in the urethra, of the nature of gleet, the discharge from which is sometimes sufficient in amount to cause the urine to yield the test of proteids obtainable with delicate reagents. Mistakes of this character, however, can usually be avoided with careful microscopical examination of the urine, not only by the absence of casts, but also by the presence of pus-cells or of the threads which are characteristic products of chronic prostatitis.

Some of the reagents used for the detection of very small quantities of proteid matter, such as picric acid, introduce fallacies of their own. Thus, for instance, the administration of alkaloids, such as strychnine, will be followed by the excretion of the alkaloid in very small quantities in the urine, but still sufficient to cause a precipitate with such a reagent as picric acid, or at any rate to cause a slight cloud; and the writer has known of cases where this has occurred and has led to the erroneous diagnosis of albuminuria. If such fallacies as these are eliminated the main difficulty still remains of distinguishing between cases of so-called functional albuminuria—that is to say, cases in which the mere presence of albumin in the urine is the sole departure from health, and cases of organic renal disease where the other symptoms of the malady are not as yet very marked. Many varieties of so-called physiological or functional albuminuria have been recognized, such as the cyclical, the postural, the dietetic, and that which is said to follow cold bathing. Recent papers by Dreschfeld<sup>1</sup> and Syers<sup>2</sup> have again drawn attention to this subject.

<sup>1</sup> Medical Chronicle, July, 1899.

<sup>2</sup> Clinical Journal, July, 1900; also Journal of Experimental Medicine, 1898, vol. iii.

Most of the cases of so-called functional albuminuria are seen in young adults under twenty-five years of age, and they are more especially seen in the case of boys under eighteen years of age. All observers are agreed that in youths albuminuria, transitory in its duration and presenting great variations from time to time in its amount, are seen, and that in some of these cases the albuminuria definitely follows exertion, in others it follows cold bathing, in others, if not caused, it is at any rate greatly increased in amount by the character of the meals. In others it is most marked on first rising in the morning. Whether all these varieties are entitled to separate names is, in the opinion of many writers, and especially Syers, decidedly in the negative. Syers, however, draws special attention to the influence of cold bathing, and more especially to sea bathing, and he states that in a large number of apparently healthy persons a plunge into the sea is followed within twenty minutes by the presence of albumin in the urine. He thinks that the habit of youths of frequently remaining in the water for a long period is not only of importance in producing this condition of functional albuminuria, but that its repeated occurrence may perhaps damage the kidney in such a fashion that it is more liable to become affected by inflammatory mischief subsequently. The fact that the exposure of the skin to the stimulus produced by cold sea-water should be followed in a considerable number of cases by the production of albuminuria is not only of interest, but is of some importance with reference to the pathology of renal diseases and the reputed influence of cold in the production of renal congestion and inflammation. It is, however, possible that such an effect as this may be produced either through the nervous system or through the vascular system, inasmuch as the effects of cold sea-water applied to the skin are at least double. On the one hand, a very powerful stimulation of the central nervous system is produced, owing to the large cutaneous area affected, and sea-water is a more powerful stimulant of nerve endings than river-water; in the second place, owing to the vascularity of the skin, the effect of the cold sea-water in constricting the bloodvessels momentarily will produce a very notable effect on the circulation. If we consider all the varieties of functional albuminuria, such as the postural, that following exertion, and that seen as a result of cold bathing, we see that all these conditions are such as might affect the circulation in the kidney, either mechanically or through the vasomotor system. If there is one fact more definitely established than another it is that very slight interference with the circulation through the kidney will cause at once the presence of albuminuria.

The changes effected in the circulation on first rising in the morning are considerable, owing to the compensatory mechanisms called into play to neutralize the effects of gravity. Gravity would tend to cause an

accumulation of blood in the abdominal viscera and in the lower limbs. This, in the healthy individual, is neutralized at once by stimulation of the vasomotor system and the production of reflex effects; thanks to which the bloodvessels of the abdomen and of the lower limbs are contracted, and thus the tendency of the blood to stagnate in the dependent parts of the body is neutralized. It is not difficult to understand that disturbances of this mechanism might readily interfere with the circulation of the kidney in such a manner as to cause albuminuria. The albuminuria that follows severe exercise and prolonged muscular fatigue might also be dependent on circulatory disturbances; but, on the other hand, in such cases as these, as also in the cases of dietetic albuminuria, it is possible that the condition is really dependent on the action of slight toxic causes and the excretion by the kidney of substances which cause a certain amount of irritation, and in this way produce albuminuria. It is well known that in fatigue considerable quantities of toxic agents are produced, and it is not very far-fetched to suppose that the albuminuria following exertion and that associated with meals may be really of toxic origin. It must, however, be admitted that our explanations of functional albuminuria, whether we look upon them as dependent or temporary derangements of the circulation or on toxic causes, are largely theoretical, and their only value is to correlate the facts. Youths suffering from albuminuria of this type do not commonly present any symptoms of ill health, but in some cases they are rather anæmic. The albuminuria is strangely intermittent, and it was for this reason, perhaps, that it was originally termed cyclical. The mere fact that the albuminuria is more marked at certain periods of the twenty-four hours than at others is a characteristic that is not confined to functional cases, but is also seen in organic diseases, and more especially in the granular kidney, where it is clearly proved that the albumin may disappear from the urine temporarily and even for considerable periods. Cases of functional albuminuria not only present no obvious symptoms of ill health, but on examination no physical signs are found pointing to the existence of the more usual accompaniments of renal disease.

The granular kidney is the renal lesion with which cases of functional albuminuria are most likely to be confounded, owing to the fact that in both cases the albuminuria is usually slight in amount. It is, on the whole, fortunate that this is the renal lesion which is most liable to be confused with the more trivial condition, inasmuch as most cases of granular kidney present physical signs in other parts of the body by means of which the condition can be recognized. The two most important groups of physical signs presented by these cases are the state of the circulation, on the one hand, and the conditions of the fundus oculi, on the other. Granular kidney is rarely present without obvious signs

of cardiac hypertrophy, if not of arterial degeneration, being present, and the examination of the optic fundus will frequently show either the presence of structural changes in the walls of the arteries or even the presence of papillitis and retinitis. The latter, however, is uncommon in cases that do not present symptoms. Usually, where retinitis is present the malady has advanced to a sufficient degree to produce symptoms such as loss of flesh, strength, etc. The wiry condition of the arteries is, however, an early sign, which may often be detected on ophthalmoscopic examination. The differential diagnosis, therefore, of cases of functional albuminuria is to be made largely on the youthfulness of the patient, the absence of a history pointing to the previous existence of renal disease, or even the absence of a history of any disease which is liable to be followed by the development of renal complications. In addition to this the most important points are the variations in the amounts and in the presence of the albumin and the absence of the physical signs implicating the vascular system. Useful corroborative evidence is afforded by either absence of casts in the urine or the presence of simple hyaline casts. Many writers state that in all forms of albuminuria hyaline casts are found to be present if the urine is examined with sufficient care; in other words, that hyaline casts are of no great diagnostic significance and certainly do not point to the conclusion that organic disease is of necessity present. The main difficulty in the interpretation of these cases of functional albuminuria is met with in cases presenting themselves for life insurance, and the usual practice in such cases is to rely on the points mentioned above, such as the absence of casts and the absence of involvement of the circulation, together with the fact that the albumin is rarely constant in amount; and the usual practice is to remit such cases for a subsequent examination.

In the vast majority of cases of functional albuminuria, or albuminuria of adolescence, the condition disappears as years go on, and although there is always a tendency to suppose that patients who have suffered from functional albuminuria in youth are more liable subsequently to contract renal disease, there is no very definite evidence in favor of this view, which is largely a matter of theory, and every practitioner knows of numerous instances, at any rate, where the condition has entirely disappeared and has not been followed by any permanent ill effects.

### ALBUMOSURIA.

Albumoses, or, as they are now called, proteoses, are not very rarely found in the urine in traces, but it is exceptional for them to be present in any very great abundance. In many cases the presence of albumoses in the urine has been regarded as evidence of the presence of true pep-

tones, but observers are agreed now that most of the cases of so-called peptonuria are really dependent upon the presence of that variety of albumose or proteose that is known as deutero-albumose. The saturation of the urine with ammonium sulphate after slight acidification of the urine with acetic acid is a most accurate method of separating albumosuria from peptonuria, inasmuch as the ammonium sulphate will precipitate albumoses and not the peptones. It is possible that in some cases the presence of traces of albumoses and peptone in the urine is dependent on changes produced in the urine after its passage, proteid matters in the fluid being converted into peptone or albumose by the traces of the digestive ferment pepsin present. Small quantities of albumoses, however, are found in the urine in a great number of diseases, and more especially in those associated with the presence of suppuration. The explanation of albumosuria in cases of suppuration is quite simple, owing to the well-known fact that pus contains considerable quantities of albumose. It is also found in such diseases as croupous pneumonia, where it probably has a similar origin to its mode of formation in suppurative diseases, being derived from the chemical changes in the exudation. It may also be found in traces where there is an effusion of a non-purulent nature, as, for instance, in pleurisy; and it has been found in a large number of acute diseases, such as rheumatism, typhoid fever, smallpox, scarlet fever, and erysipelas. In all these cases, however, the quantity of albumose which is found in the urine is small and only sufficient to give the characteristic biuret reaction with copper sulphate and caustic potash. In exceptional cases it occurs in the urine in great abundance, and one such case has been recently described by Bradshaw.<sup>1</sup> The case described by Bradshaw is in many respects similar to the one originally described by Bence Jones, who was the first to allude to the presence of albumoses in the urine, in the year 1848. Bradshaw's case is remarkable not only from the very large quantity of albumose which was present in the urine, but also from the fact that this proteid matter was spontaneously precipitated. This only occurs in rare instances. Bradshaw describes the urine in his case as clear when it was passed, and on inspection it presented no abnormal change except that it was remarkably viscid and tended to form a persistent froth. Urine passed in the middle of the day was very frequently turbid when voided, and presented an appearance resembling that of milk, and on standing it deposited a copious white sediment. This sediment under the microscope was seen to be amorphous, consisting of minute, structureless spherical particles, and when collected on a filter it gave the xantho-proteid and other proteid reac-

<sup>1</sup> *Medico-Chirurgical Transactions*, vols. lxxx. and lxxxii.



tions. It was almost insoluble in cold water and in dilute solutions of common salt, but it dissolved to some extent in warm water. The urine was free from casts, and had a specific gravity of 1015 to 1022. When heated on a water-bath it began to get turbid at 50° C., and the dense white precipitate began to settle down at 60° C. According to Bradshaw, the precipitate which formed at 60° C. was identical in its essential characters with the white sediment which was deposited from the urine from time to time. The precipitate formed at 60° C. was not a true heat coagulum, as it underwent partial re-solution if the urine were heated to the boiling-point. Nitric acid when added to the urine caused a precipitate which was partially dissolved by heating, returning on cooling; in other words, yielding the characteristic reaction of an albumose. According to Bradshaw, from 10 to 12.9 grammes of this substance might be excreted in twenty-four hours. Bradshaw gives an account of the few cases which have hitherto been described in the literature where a substance similar to this was excreted in the urine in large amounts. In all, some seven cases have been previously described since the first one recorded by Bence Jones in 1848. Kuhne and Huppert described such a case, and they considered that the substance present in the urine was hetero-albumose. Matthes concluded that the body in his case was not hetero-albumose, but a substance allied to this and not identical with any other known body. Bradshaw's case was remarkable not only from the fact that the albumose was present in such large amount, but also that it caused turbidity of the urine when passed. He considers that the substance was not hetero-albumose, but a peculiar body which is not identical with any other known compound, and that it differs from hetero-albumose in being soluble in distilled water, and from the other albumoses formed during digestion in being coagulated by heat. In six out of the seven cases recorded in the literature, where this body was excreted in such large amount in the urine, disease of the bones in some form or other was present. In Bence Jones' and Kuhne and Huppert's cases softening of the bones was described. In Stokvis' case post-mortem examination showed that the bone-marrow was replaced by red, gelatinous tissue; and as Bradshaw records, in Matthes' case and Senator's case there was evidence of the presence of myelogenous sarcoma. Bradshaw's patient came under observation, first of all, with vague symptoms of ill health, and the substance was detected in the urine owing to the turbidity of the fluid when passed; this had been observed at intervals for some years, and more especially during the last year prior to his seeking advice. When first seen, in the year 1896, he presented no physical signs of disease, with the exception of the passage of the turbid urine; but toward the close of 1897 the patient began to have severe pain and tenderness about the ribs, sternum, and

back, and early in 1898 the bones of the chest became soft, and several spontaneous fractures of the ribs took place. He died in August, 1898, and the peculiar character of the urine persisted to the end. Post-mortem examination showed that the kidneys presented the appearance of slight chronic interstitial nephritis, and that the medulla of the ribs and dorsal vertebræ and of the sternum was replaced by a bluish-red, semi-solid pulp. The bones had undergone great diminution in thickness, so that the ribs in many cases were reduced to a mere shell of bone. An extract made from the fresh marrow showed that albumoses were present in this material. Microscopical examination of the marrow of the bones removed showed that the normal marrow was replaced by a structure which might have been described as a round-celled sarcoma or as a lymphoma. Bradshaw looks upon his case as one of multiple myeloma where the osseous tissue has undergone atrophy as a result of the presence of the growth. Bradshaw points out that the records of the other cases of the malady described show a general resemblance in their morbid anatomy, but the appearances presented by the medulla of the bones in different cases are not identical. In some cases analogous changes in the bones have occurred without the presence of albumosuria. Bradshaw considers that the condition is entitled to the term myelopathic albumosuria, and that, although albumosuria does not occur with all forms of bone disease, there is a distinct disease characterized by the presence of albumoses in large amount in the urine, together with these changes in the medulla of the bones.

Although it is uncommon for large quantities of albumoses to appear in the urine, the writer has seen one case where albumoses not only occurred in large amount in the urine of a woman suffering from an ovarian cyst, together with granular kidney, but in this case the amount of albumoses was so large as to lead to a slight spontaneous precipitation, somewhat similar to that described in Bradshaw's case; and in another case of chronic renal disease very large quantities of albumoses were present, together with the ordinary coagulable proteid. There can be no question that albumosuria to a marked extent may be a most characteristic feature of certain diseases of the medulla of bones, and also that cases of so-called osteomalacia may be confounded with multiple myeloma or even with ordinary malignant disease of the bones. The main interest of Bradshaw's case lies in the fact that the albumosuria was present for many years prior to the onset of the marked symptoms pointing to the bone disease, and the presence of albumoses in the bone-marrow may perhaps throw some light on their excretion in the urine. It must, however, be remembered that albumoses are not uncommonly products of post-mortem change, as, for instance, in the spleen, where albumoses may be found a few hours after death; but if the spleen be

removed from animals and examined so rapidly as to avoid any post-mortem changes these bodies are absent. For this reason the exact explanation of the albumosuria associated with disease of the bones, either of the nature of osteomalacia or of myeloma, cannot as yet be given. The abundant albumosuria which is rarely associated with granular kidney is also very difficult of explanation, although it is possible that here it is of intestinal origin—that is to say, that, either as a result of anomalous digestive or absorptive processes, albumoses are present in the blood and are excreted in the kidney. As mentioned before, the albumosuria complicating microbic and suppurative diseases generally is capable of simple explanation.

### ALKAPTONURIA.

Among the substances which may be mistaken for sugar in the urine when this fluid is tested with Fehling's solution, alkapton must be included. It is, however, one of the rarer sources of fallacy in the recognition of glycosuria, and is by no means so common as the presence of an excess of uric acid, creatinin, glycuronic acid, etc. Garrod<sup>1</sup> records the results of an investigation in four cases of this rare condition, and he gives also a valuable summary of our knowledge of alkaptonuria at the present day. The essential features of the urine in this condition, as enumerated by Garrod, are, first, that although of normal appearance when passed, the urine rapidly acquires a deep brown color, and ultimately becomes black on exposure to air; second, the brown color is greatly intensified by alkalis, and its development is accompanied by absorption of oxygen; third, the urine reduces Fehling's solution with the aid of heat, and actively reduces ammoniacal silver nitrate solution in the cold. The urine has neither dextrorotatory nor levorotatory power. The fermentation test yields negative results, and fabrics moistened with the urine become deeply stained on exposure to air.

Garrod's summary of the clinical features of alkaptonuria is based upon an analysis of thirty-one cases collected by him from the literature and from those observed by himself. Alkaptonuria is considerably more common in males than in females, as the series included twenty-three males and only eight females; and in the great majority of cases the condition came on in early childhood. In seventeen of the cases observed it began in infancy, and in some cases it was noticed on the day following birth. Alkaptonuria seems to be a family disease, in that several members of the same family are apt to present it; but Garrod knows of no instance in which it was transmitted from one generation

<sup>1</sup> *Medico-Chirurgical Transactions*, vol. lxxxii.

to another. In one case three members out of a family of four were affected; in another, four out of a family of fourteen. In a few cases alkaptonuria has been observed intermittently, and in one recorded case a diabetic patient passed alkapton in the urine on one day only. Although the condition is sometimes associated with more or less serious diseases, such as diabetes, phthisis, gastric ulcer, and pyonephrosis, the condition is one which does not, as a rule, cause any inconvenience, even when lifelong, nor any injurious effect upon the health of the patient. The most important fact with reference to the condition is the liability for it to be mistaken for glycosuria. There has been some difference of opinion among observers, since the first description of alkaptonuria in 1859 by Bodeker, as to the exact nature of the substance which is present. Originally it was thought to be pyrocatechin. Later, in 1882, Walter Smith thought that in all probability the substance was protocatechuic acid; and in 1886, Kirk isolated two acid substances—uroleucic and uroxanthic—in these urines. In 1891, Wolkow and Baumann extracted from the urine a crystalline acid, to which the name of homogenticinic acid was given, and they showed that the reducing power of the urine was dependent on the presence of this body.

As Garrod points out, all subsequent observers who have investigated cases of alkaptonuria have demonstrated the presence of homogenticinic acid, and in some cases one of the acids separated by Kirk, and known as uroleucic acid, was demonstrated. Wolkow and Baumann also demonstrated the fact that tyrosin administered to the alkaptonuric individual increased the amount of homogenticinic acid in the urine, whereas it did not do this in the normal individual. A meat diet has a similar result. It would seem from these observations that tyrosin is the substance that gives rise to alkaptonuria, and, inasmuch as this body is formed in the alimentary canal, it has been thought by some that alkaptonuria is dependent on intestinal decomposition due to the activity of microbes. This view, however, has not received much support, owing to the fact that the alkapton bodies have not been found in the alimentary canal, and also because treatment with intestinal antiseptics has no influence on the condition. Garrod describes four cases, which he examined fully, where he found homogenticinic acid in the urine. He examined two cases with the view to the detection of uroleucic acid, and failed in both instances, and, therefore, he was inclined to look upon this substance as a by-product.

Alkaptonuria would seem to be dependent on a disturbance of the normal metabolism of bodies of the tyrosin group, although the evidence is not complete that the origin of the substance is entirely dependent on intestinal decomposition.

**Cystinuria.** Another rare constituent of the urine—cystine—has been the subject of investigations during the last year by Simon,<sup>1</sup> and Cammidge and Garrod.<sup>2</sup> Both these observers have been engaged more especially with the relationship existing between the presence of diamines in the urine and the presence of cystine. In a small number of cases of cystinuria, diamines—namely, cadaverine and putrescine—have been found both in the urine and in the feces. In Garrod and Cammidge's observations the diamine excretion was intermittent, and in the case observed by them there was no diamine excretion for a period of twenty-three days. These observers draw attention to the fact that the presence of these bases in the urine can only be excluded after a very prolonged and tedious examination. They found cadaverine in the urine and putrescine in the feces; and Cammidge and Garrod conclude that inasmuch as the diaminuria is intermittent, it is probable that the systematic examination of the excreta in cases of cystinuria would lead to the recognition of diamines in a greater number of cases. They have failed to detect the presence of diamines in cases of puerperal eclampsia, chronic diarrhoea, diabetes, Addison's disease, and gout; but they obtained some evidence that these substances were present in a case of alkaptonuria. Cammidge and Garrod failed to obtain from the feces any organism that was capable of forming diamines in the nutrient medium in which it was grown. The presence of diamines in the urine of cases of cystinuria has led to the view that these cases are of intestinal origin; but Simon, in an elaborate consideration of the subject, suggests that both the formation of cystine and of such a diamine as putrescine may occur from disordered proteid metabolism; and he considers that the presence of diamines is neither the cause nor the effect of the cystinuria. He considers that both the diamines and the cystine are due to a metabolic anomaly in which the power of oxidation of some or of all the body tissues is at fault; and he adduces in support of this view not only a considerable amount of chemical evidence explaining how the cystine and the diamines may be formed from a proteid molecule, but draws attention also to the fact that cystinuria is liable to occur in families, and that in some respects the disease may be placed in the same category as gout, rheumatism, diabetes, and obesity; and that, according to the observations of Moreigne, the ratio of urea nitrogen to total nitrogen is diminished. Further, that whereas the total amount of sulphur is not increased, the absolute amount of completely oxidized sulphur is diminished. Simon considers that the older observations, in which cystinuria was held to be associated with chlorosis and

<sup>1</sup> American Journal of the Medical Sciences, 1900.

<sup>2</sup> Journal of Pathology, 1900.

anæmia, are of some importance, and he believes that the condition is dependent on the retardation of the normal metabolic processes ; and it is probable that the liver is the organ which is most concerned in the process.

### **SKIN ERUPTIONS OCCURRING IN BRIGHT'S AND OTHER RENAL DISEASES.**

The relationship existing between the skin and the kidney is supposed by many to be at least threefold. First, that changes produced in the circulation of the skin or in the nerve elements of the skin by the action of cold may produce, reflexly, circulatory disturbances in the kidney, and perhaps even inflammation. Second, various affections of the skin are liable to be complicated secondarily by the development of renal disease, and some observers have thought that the suppression of the functions of the skin, more especially the sweat secretion, might entail the retention in the organism of toxic or injurious substances, and that the excretion of these by the kidney might actually cause nephritis. Third, that diseases of the kidney, and more especially toward their termination, are associated with the development of certain skin eruptions. The part that the skin plays as a factor in the etiology of renal disease is, however, by no means so clearly established now as it was formerly thought to be, notwithstanding the intimate interdependence that exists between the secretion of sweat and that of the urine. Although, as a result of cold, the quantity of urine secreted is increased in a striking manner, physiologists have hitherto failed to demonstrate any very close relationship between the vascular mechanism in the skin and that in the kidneys, and, experimentally, certainly the application of cold in the form of ice-bags to the skin of animals does not materially affect the circulation in the kidney, as determined by oncometric observations. It is possible, however, that the great effects produced on the renal secretion by external cold are really produced through the nervous system, although no direct evidence of this exists from an experimental stand-point. It is probable, however, that the action of cold as an etiological factor in the production of renal disease has been exaggerated, as it is very rarely that cold produces renal disease without the operation of some other cause, usually a toxic one. Thus, the combination of chronic alcoholism and exposure to cold is a fertile cause of Bright's disease, and most observers consider that exposure to cold during the course of an acute specific fever, or early during its convalescence, may act in the same way. It is quite possible that in these cases the mechanism is really complex. Thus, cold may depress the resistance of the tissues, so that a toxic agent is able to produce effects which it would fail to do with more resistant tissues, much in the same

way that cold acts as a supposed cause of pneumonia. On the other hand, the cold may produce its effects by diminishing the excretion of sweat, and toxic substances which are present in the organism and which should be excreted *via* the sweat may under these circumstances be excreted through the kidneys, and in this way lead to the production of renal disease. It has long been noticed that in Bright's disease and other renal diseases the skin is prone to be dry and harsh and the secretion of sweat exceedingly scanty and difficult to promote. The mere non-secretion of sweat, however, by the skin cannot be looked upon as a cause of renal disease, inasmuch as there are many conditions, especially in febrile diseases, where the secretion of sweat is entirely arrested without the production of any renal complications. Some lesions of the skin, such as burns and certain skin diseases, as, for instance, pityriasis rubra, are held to be definite causes of renal disease. In the case of the nephritis following burns it is probable that the renal lesion is dependent upon the absorption of toxic bodies formed at the seat of the burn and their subsequent excretion by the kidney. In the case of pityriasis rubra the relationship is more complex, because although many dermatologists consider that the renal lesion is the sequel to that of the skin, yet in some cases chronic interstitial nephritis—*i. e.*, the granular kidney—has been found in an advanced stage in such cases, giving rise to the idea that the renal lesion has preceded the skin affection. There is, therefore, some doubt, both as regards the relationship of the skin to the kidney in the etiology of renal disease and also as to the production of renal lesions as a sequel of skin diseases; but it is certain that extensive skin disease may exist for many years without the production of any renal lesion. This is notably the case, for instance, in general eczema, where the disease may exist for years without the supervention of any renal complications. On the other hand, the third relationship existing between the skin and the kidney, namely, that skin diseases occur as a complication of renal lesions, is universally admitted, and the number of affections which may occur under these circumstances is considerable. As mentioned above, in almost all cases of chronic renal disease the skin becomes dry and harsh and assumes a sallow color. This dryness of the skin is often so great that the sweat cannot be elicited by hot-air baths or even by the action of such a powerful drug as pilocarpine. Pigmentation of the skin is also not a very uncommon complication of renal disease. Pigmentation usually assumes the characters that are associated with the existence of such chronic diseases as tuberculous peritonitis, and the skin becomes of a brownish hue, simulating that seen in Addison's disease. The distribution of the pigmentation is not so general nor so characteristic as that found in the latter malady. In exceptional cases, and more especially in cases of contracted

white kidney and the granular kidney, this pigmentation of the skin is more marked, more general in its distribution, and simulates much more closely that seen in Addison's disease, so that the writer has known that error of diagnosis to have been made, where the autopsy has shown the presence of Bright's disease and the absence of Addison's disease. As far as is known, the pigmentation that is occasionally seen in chronic renal disease never affects the mucous membranes.

Purpura is also a common accompaniment of renal disease, and again more especially of the contracted kidney. The pigmentation of the skin described above must be looked upon rather as a result of the grave nutritional disturbance produced by the renal lesion than as dependent on any close relationship between the skin and the kidney, and the purpura so frequently seen in renal disease is to be regarded as a result of the morbid state of the blood and of the bloodvessels present in renal disease than as dependent upon any special disorder of the skin. The tendency to hemorrhage in renal disease is general and wide-spread, and these hemorrhages may occur not only in the skin and in the retina, but also in the serous cavities and from the mucous membranes.

As regards the other affections of the skin associated with renal disease and occurring as complications, the relationship is more intimate, and they may perhaps be looked upon as due in some measure to the interdependence existing between the functions of the skin and those of the kidney.

Skin affections in renal diseases are more common and more characteristic in the chronic forms of the disease and in their later stages, but some affections have been described as characteristic of or at any rate as associated with the earlier stages of renal disease.

Pruritus may perhaps be looked upon as a complication of the earlier stages of renal disease; and Thursfield<sup>1</sup> has recently drawn attention to its occurrence. Pruritus is a condition which is associated, however, with many constitutional disorders in which toxæmia plays a part, and is, as is well known, more especially characteristic of diabetes and of jaundice. It may, however, be equally well marked in renal disease, and in exceptional cases it has been noticed as an immediate antecedent to the onset of uræmia. Some French observers, more particularly Delafour, look upon marked pruritus as a symptom of sufficient importance as to assist in the diagnosis of granular kidney. Certainly in all cases of marked pruritus occurring in middle-aged persons the urine should be systematically examined, not only for sugar, but also for albumin, as the granular kidney is a disease which is nearly always exceedingly insidious and difficult to recognize in its early stages. Some

<sup>1</sup> Medico-Chirurgical Transactions, vol. lxxxiii.



writers have held that the presence of pruritus associated with a general failure of health, together with the presence of a trace of albumin in the urine, is sufficient to make the diagnosis of granular kidney. Thursfield has shown that pruritus may occur, however, not only in the granular kidney, but also in cases of chronic nephritis, and that in exceptional cases it may be the only symptom for which the patient seeks advice. So many varieties of renal disease are liable to be overlooked, owing to the apparently trivial nature of the symptoms for which the patient seeks advice that it is of importance to recognize that persons suffering from such a grave disorder may come complaining of such a comparatively trivial symptom as pruritus.

Urticaria of a severe type may also occur in cases of Bright's disease, and is also sometimes associated with the presence of uræmia. Urticaria is a skin affection which is undoubtedly of toxic origin, as it is readily produced by certain articles of diet, and is also seen as a very constant phenomenon with the modern treatment of disease by antitoxins; and its occurrence in renal disease, therefore, is not surprising, and may be taken as unquestionably dependent on the presence of some toxic substance. The nature of the toxic body, however, is quite unknown, and it is certainly not urea, as is well known from the observation of Bartels, who many years ago described the excretion of very large quantities of urea from the skin, in sufficient amount for the substance to crystallize on the skin, without the production of any eruption.

The relation of eczema to renal disease is more problematical, since both eczema and renal disease are very common maladies, and, therefore, there is great probability of the two diseases coexisting in the same patient. Eczema, even in its most severe forms, may exist for many years without the production of any renal complication.

The other skin eruptions which are seen in renal disease usually occur in the later stages of the malady, and in many cases are associated with the presence of uræmia, so that they have been described as uræmic complications. They may be erythematous, bullous, or desquamative. The most characteristic is the erythematous variety, which has been spoken of as an *erythema uræmicum*, or sometimes as *erythema papulatum uræmicum*, and has been described by many observers, the descriptions in all cases agreeing closely. The eruptions at the outset consist of papules of a bright red color interspersed with some maculæ. According to Lancaster, the eruption is most likely to begin on the extensor surfaces of the hands and feet. The maculæ and papules soon become confluent and involve other parts of the body, including the face, and they also become darker in color; subsequently to this desquamation takes place. In some cases the eruption may assume the appearance of a general eczema, or it may become pustular. All

observers agree that this eruption is especially liable to be associated with uræmia, and that it may not only be a precursor of uræmia, but that in all cases it is of ill-omen, and that the patient usually dies within a few days of the onset of the rash, or, at the outside, within a few weeks.

Thursfield quotes a French writer who describes a case of chronic parenchymatous nephritis where two independent attacks of uræmic coma were associated with each development of the uræmic symptom, disappearing on each occasion with the subsidence of the uræmia. Thursfield has been able to collect thirty-six recorded cases of this affection in the course of the last twenty-five years. Bullous eruptions are occasionally seen in renal disease, and several observers have quoted cases of chronic pemphigus which terminated in death from uræmia associated with the presence of granular kidney. Pityriasis rubra, or eruptions resembling it, are also occasionally seen associated with Bright's disease, but in some cases, as mentioned above, the renal lesion is probably the result of the skin disease rather than the cause; and this is more especially probable, inasmuch as in some cases the renal lesion is developed quite late in the history of the case. Thursfield also describes some cases of general exfoliative dermatitis associated with intense pruritus, with the formation of bullæ on the trunk and limbs and occurring with fatal uræmia.

Most observers agree that there is at least one form of erythema that is specially suggestive of uræmia, and in this the disease begins in the form of disks the size of the thumb nail, which speedily coalesce into a general eruption, accompanied by free desquamation. The erythema accompanying acute uræmia may present a good deal of variety in its characteristics. Thus it may be papular or scarlatiniform, and the writer has seen at least one case where the character of the generalized erythematous eruption was closely similar to the eruption of scarlet fever. The rash, however, occurred in the last stages of chronic nephritis accompanied by uræmia.

All these different varieties of skin eruptions are probably dependent on the action of toxin, and it is at any rate probable that the toxic substance is not simply one of the retained normal constituents of the urine, but is more likely to be an abnormal substance formed as a result of the deranged metabolism.

These rashes are more especially associated with uræmia, and do not occur, as far as is known, in calculous suppression, where all the urinary constituents are retained.

**PERICARDITIS IN RENAL DISEASE.<sup>1</sup>**

Renal diseases, and especially Bright's disease, are fatal very commonly from the complications ensuing during the course of the malady, and among the most serious of these may be enumerated the so-called secondary inflammations. It has often been pointed out that in acute infections the original infection very rarely is actually the cause of death in fatal cases, secondary infections playing a very large part. The same is true with regard to such chronic affections as renal diseases.

The secondary inflammations in kidney diseases may affect either the serous membranes or such organs as the lungs; and among the serous membranes the pericardium is one very often attacked. So much is this the case that Bright's disease is looked upon as one of the main etiological factors in the causation of pericarditis. Pericarditis is not only of importance in Bright's disease, owing to the frequency of its occurrence, but also owing to the fact that it is usually a very serious complication, and thus the underlying renal malady not only plays a part in determining the onset of the pericarditis, but it also influences to a very great extent the course and termination of the malady; so that all writers are agreed that the pericarditis of Bright's disease is a very much more serious malady than the pericarditis of rheumatism.

Although all writers are agreed as to the severity of the pericarditis complicating renal disease, they are by no means agreed as to the frequency, and still less as to the nature, of the illness. English writers, such as Dickinson and Taylor, look upon pericarditis as an exceedingly common complication of Bright's disease; and some English writers have thought that Bright's disease was a more frequent predisposing cause of pericarditis than all the other predisposing causes of the malady put together. It has been said to occur in 30 per cent. of the cases of chronic Bright's disease and granular kidney. Rayer thought the incidence of the disease very much less than this, and put it as 0.5 per cent.; Frierichs at 4 per cent.; Buhl at 35 per cent. As Chatin points out, these great differences in the statistics of the prevalence of the disease must depend to a great extent on what the different writers recognize as pericarditis; in some cases thickening and opacity of the pericardium are included; in others only the more obvious cases where there is effusion have been considered. The same difficulty presents itself clinically as well as pathologically with regard to the recognition of pericarditis in renal diseases, since so many of the cases run a latent course. If these cases of latent pericarditis and the cases where, in the post-mortem room, only opacity and thickening of the pericardium are

<sup>1</sup> *Revue de Médecine*, Juin, 1900, No. 6.

noticed are put aside, there still remains a considerable number of cases of acute or subacute pericarditis, with or without effusion, associated in some manner with renal disease. Not only is this malady common in all forms of Bright's disease, but it is especially associated with the granular kidney or the so-called raspberry kidney; both acute and subacute pericarditis are seen as not uncommon complications of this affection. Two main theories or views have been held with reference to the etiology of the malady.

A number of writers have drawn attention to the not uncommon coexistence of pericarditis with the phenomena of uræmia, and Lance-reaux may be mentioned as one who drew attention to this association. Other writers, and more especially Lecorché and Talamon, have been more struck with the association of pericarditis with other inflammatory complications such as pneumonia and pleurisy. So it has come about that two varieties of pericarditis have been held to be associated with Bright's disease: one the so-called toxic or uræmic pericarditis, and the other a secondary pericarditis dependent on extension of inflammation from other parts. Bright himself and the older writers, such as Bartels, looked upon pericarditis as of toxic origin, and they deduced this more especially from its association with uræmia. Observations on the toxic effect of urea and other substances present in the urine have, however, quite failed to yield any support to this view, and the injection even of large quantities of urea into the pericardium quite failed to reproduce anything analogous to pericarditis, notwithstanding the well-known fact that in certain animals, as, for instance, birds, ligature of the ureters is followed by the deposition of considerable quantities of uric acid in the pericardium. Notwithstanding the failure of all experimentation directed to show that pericarditis is of toxic origin, numerous writers still look upon it as of this nature and talk of it clinically under the name uræmic pericarditis. There is no doubt that in some cases there is a very close association between the two phenomena, and the onset of acute uræmia in chronic renal disease may be synchronous with the development of an acute or subacute pericarditis.

Banti has investigated a number of cases of pericarditis occurring in chronic renal disease with reference to the presence of micro-organisms, and in a series of four cases very carefully observed he failed to obtain any evidence of the presence of micro-organisms. In all of Banti's cases the underlying renal disease was chronic, but the pericarditis was acute, the first case having appeared eight days before death, and the second case four days before death. Banti's observations were singularly complete, from the fact that he not only made stained preparations of the exudation, but he also attempted to obtain cultures from them; and, further, he injected the material into guinea-pigs and

rabbits, but in all cases he failed to obtain any evidence of the presence of any micro-organism. Banti also, in the last two cases, found that the blood of the heart and the spleen juice were also sterile. Bosc, in the examination of one case of acute pericarditis occurring in a case of chronic renal disease associated with hypertrophy of the heart, found the pneumococcus present in the exudation. Several other observers beside Banti have, however, failed to detect micro-organisms in the acute pericarditis supervening in chronic renal disease. Chatin, who deals with the literature associated with this malady, has examined four cases in a similar manner, but in addition to searching for micro-organisms in the pericardium, he has determined the toxicity of the blood serum. In three cases a bacteriological investigation of the effusion was made, and in four cases observations on the toxicity of the blood serum were conducted. Of the three cases where post-mortems were obtained, in two granular contracted kidney was present, and in the third chronic Bright's disease. In all three cases the pericardial effusion failed to show the presence of any micro-organisms. In one of these the pericarditis was acute, of the sero-fibrinous variety; in the second case it was subacute, and in the third it was chronic.

We must conclude from these observations, together with those of the other authors quoted above, that at any rate in a large proportion of cases the pericarditis of Bright's disease, even when acute, does not show the presence of micro-organisms; and this would certainly seem to support the view that it is of toxic origin. This view does not receive much support, since Chatin's observations dealing with this part of the subject are very difficult to understand, since in all the cases in which he investigated the toxicity of the serum he got the same result, namely, that it was less toxic than normal, whereas naturally, with the current theories with reference to the nature of uræmia, it would be supposed that the toxicity of the serum would be greatly increased in this condition. Chatin concludes that the absence of microbes in the pericardial effusion clearly establishes the existence of what he calls an aseptic non-microbic pericarditis in Bright's disease. Chatin considers that the normal toxicity of human serum when injected into the rabbit is to be represented by 17 c.c. of serum per kilogramme of rabbit. The numbers he obtained in his observations were 28 c.c., 48 c.c., and 22 c.c. per kilogramme; that is to say, in all cases the serum was less toxic than normal, and in one case very much less toxic. In addition to investigating the toxicity of the blood, he also made observations on the toxicity of the pleural effusions, and here he obtained similar results. He concludes that neither in the circulating blood nor in the fluid of pleural effusions can toxic substances be demonstrated, even during the acute stage of uræmia.

Great contradictions, however, are found in the records of different observers of the toxicity of the blood serum in uræmia. In eclampsia Tarnier and Chambrelent have shown that during the convulsive stage the toxicity of the blood is greater than normal. But other observers, Baylac, Guinard and others, in addition to Chatin, have shown that in the uræmia accompanying chronic nephritis the serum may be less toxic than normal; and there is one remarkable case observed by Dumaret, where the serum was less toxic in a fatal attack of uræmia than it had been in the same case in a former attack from which the patient had recovered. At the present time the matter rests in this state, and these observations would certainly seem to throw some doubt on the ordinarily accepted views that uræmia is of toxic origin. Still, Chatin states, and most physicians will agree with him, that uræmia must be looked upon as of toxic origin, notwithstanding these contradictions and difficulties in determining the nature or even the presence of toxic bodies in uræmia. He concludes, finally, that pericarditis in Bright's disease is, in the great majority of cases, of non-bacterial origin, and that it is only in exceptional cases that it is associated with the presence of microbes, and this notwithstanding the fact that observations on the pericardial and pleural effusions accompanying the pericarditis do not yield any conclusive results pointing to these fluids containing toxic substances.

### **MODE OF ACTION OF CERTAIN POISONS ON THE KIDNEY.**

The pathology of nephritis and of Bright's disease is getting more definite with the progress of our knowledge with reference to the nature and the action of organic poisons, and more especially those of microbic origin. Hence it is that Bright's disease is looked upon more and more every day as an affection that is produced by the action of toxic bodies. In a number of cases this is self-evident, as where the malady is the sequel of certain occupations, such as workers in lead, and also where it results from chronic indulgence in alcohol. It is, however, possible now to classify the action of toxic bodies on the kidney structures much more accurately, and they may even be divided up to a great extent according to the nature of the action that they produce, since there is a certain amount of evidence to show that many poisons have a differential action on the kidney structures, singling out certain portions of the kidney, at any rate, for their maximum action. According to Lindemann,<sup>1</sup> it is possible to divide the toxic bodies acting on the kidney into three groups, according to the preponderant effect produced by a typical member of

<sup>1</sup> *Annales de Pasteur*, 1900, No. 2.

each upon certain structures of the kidney ; but Lindemann, in common with all other observers, would consider that the differential action of poisons on the kidney is at the most a partial one, and that the dividing up of nephritis into glomerulo-nephritis, tubal nephritis, and interstitial nephritis is in great measure artificial. The most that can be meant by glomerulo-nephritis is that the lesions produced in the glomeruli are rather more marked and form a more prominent result than those in the tubules or in the interstitial tissues, and there is no such thing as a pure glomerulo-nephritis, or a pure tubal nephritis, or even a pure interstitial nephritis.

According to Lindemann, three groups of renal poisons can be recognized, and the first group consists of those which produce glomerulo-nephritis to a marked extent. A typical example of these poisons is afforded by the action of cantharidine, and in pathology the virus of scarlet fever produces almost precisely similar results. The second group of renal poisons is that which consists of the metallic salts and the oxides of the heavy metals, the prolonged action of which causes a coagulating necrosis of the cells of the convoluted tubules. Another member of this series which is of importance in laboratory investigations is chromic acid, but from the pathological point of view the heavy metals are of more importance. A third group of renal poisons consists of animal and vegetable toxic bodies, such as serpent poison, abrine and ricine, and also, as has been recently shown, the blood of certain fish, more particularly of the eel. These complex organic poisons produce by their action a degeneration of the epithelial cells of the kidney, characterized by degeneration of the protoplasm of the renal cells and the formation of vacuoles ; but the nuclei of the renal cells persist, and in this way the condition is in sharp contrast to that which is produced by the action of the heavy metals. Lindemann has carried out some observations on the action of vinylamine, a primary amine of vinylic alcohol. This substance has a general toxic action which need not detain us here, but in addition it has a very special action on the kidney, both when given so as to produce acute poisoning and also when administered in smaller doses so as to cause a more chronic intoxication. Albuminuria is produced on the first day of its administration, even when given in very small doses, and the urine contains on that and the following days an abundant deposit of granular casts and leucocytes, together with a small number of blood-corpuscles. During the initial stage of the action of the poison the urine is increased in quantity, and is dilute and clear ; but with the progress of the action of the poison the quantity diminishes, and death is preceded by a period of complete anuria. Together with these local actions of the substance on the kidney, the action of vinylamine is such as to cause very great

wasting—loss of body weight—which is especially seen in cases of chronic poisoning. It is possible that this action is a direct one, owing to the substance interfering with the metabolic processes; but, on the other hand, it is possible that it is dependent really on its renal action, since both experimental lesions of the kidney, such as the removal of large quantities, and diseases of the kidney where the quantity of renal tissue is seriously diminished, cause very great wasting. The loss of weight that is seen as a result of the action of vinylamine resembles very closely that seen experimentally after the removal of three-fourths of the total kidney substance, inasmuch as the animals lose from 40 to 45 per cent. of their body weight, notwithstanding the fact that the appetite is not lost. The renal lesions that are produced are not very obvious to the naked eye, and on microscopical examination they are seen to vary according to the duration of the toxic action. In acute cases the kidney is acutely congested, and the glomeruli are dilated and the capillary tufts gorged with blood. The capsules of Bowman are filled with epithelial masses, and the protoplasm of the cells of the convoluted tubules loses to a great extent its characteristic structure and becomes more transparent, but the nuclei undergo no change. The epithelial cells of the convoluted tubules often become vacuolated, and they assume irregular shapes. Lindemann is of the opinion that the microscopical appearances give rise to the impression that the protoplasm undergoes a progressive solution, and that fluid masses of it pass into the stream of urine. If the toxic action is more prolonged glomerulo-nephritis becomes more intense, and the tubules are filled with granular masses. The cellular detritus passes into the urine and is excreted. Lindemann notes that the straight tubules do not present any marked changes. Where the toxic action is still more prolonged, so that the animal survives from ten to twenty days, the glomerulo-nephritis diminishes in amount, the convoluted tubules become filled with casts, and the nuclei disappear from an increasing number of the cells. The formation of casts is extraordinarily abundant, and they are found not only in the straight tubules, but also in the convoluted. The interstitial tissue does not present any changes, and the action of vinylamine differs from that of most other renal poisons in the fact that even in chronic poisoning there is no development of cirrhosis. The action of vinylamine, then, resembles very closely that which is produced by bacterial toxins and by animal and vegetable proteid poisons. On the other hand, it resembles that of cantharides, owing to the severity of the glomerulo-nephritis produced. Lindemann draws attention to the fact that vinylamine is a substituted ammonia, and, like other substances of this group, it is a renal poison; and he states that renal lesions similar to those produced by its action are also seen to follow



the administration of cadaverine and putrescine. These results are of great importance to the pathologist, and in some ways would simplify our ideas with reference to the relationship existing between renal disease and intestinal putrefaction. Lindemann not only deals with the action of vinylamine on the renal structures, but he details some remarkable experiments as regards the action of serum on the renal structures. Claude Bernard, many years ago, showed that the injection into one animal of the blood serum derived from another was capable of causing albuminuria of longer or shorter duration. In Bernard's experiments the serum of dogs was injected into rabbits. These and other similar observations led to the foundation of the well-known view of Bright's disease that was advocated by Semmola and others, that the disease was originally a blood disease, and that the changes in the kidneys were produced by the action of some anomalous constituent of the blood. It was even thought at one time that the proteid matter that was excreted in renal disease was very often some anomalous proteid not normally present in the blood. Semmola, for instance, performed a number of experiments regarding the results following the injection of egg albumen, and he and others at one time thought that the albuminuria produced in this way was dependent on the introduction into the blood-plasma of an anomalous proteid which was subsequently excreted. At one time this view of Bright's disease was very largely held, but when it was shown that the albuminuria which followed the injection of egg albumen was an albuminuria dependent on the presence of serum albumen and serum globulin in the urine—in other words, that the egg albumen only acted as an irritant substance on the kidney, impairing its efficiency as a filter and allowing the proteid of the blood-plasma to be excreted—this view of the nature of Bright's disease was gradually abandoned, and at the present time no pathologist looks upon the disease as primarily dependent on an alteration in the composition of the proteid elements of the blood. Lindemann's results, however, are of a very extraordinary character, and will, at any rate, attract the attention of pathologists. He draws attention to the fact that Weiss has repeated Bernard's experiment, and has shown that not only does the blood serum of a different species of animals cause albuminuria when injected into the rabbit, but he states that the serum of an animal of the same species but of another sex may produce the same results. Weiss claims that in the case of the rabbit the most toxic serums are those of the cat and of the guinea-pig; that the injection of these serums into rabbits may be followed by death, and that in all cases the quantity of albumen secreted in the urine is less than that which was present in the injected serum. Lindemann states that the normal serum, when obtained from another species of animal, only acts as a renal poison in

exceptional cases, and that this is true in the case of the action of the serum of the guinea-pig on the rabbit's kidney. Lindemann often failed, even when he injected doses as large as 8 c.c. of serum per kilogramme of rabbit, to produce albuminuria, and so in order to increase the toxic action of the serum on the kidney he was led to perform some experiments on the line of those recently carried out by Metchnikoff, Bordet and Ehrlich. Lindemann attempted to increase the toxic action of the serum on the kidney by introducing into the organism kidney substance, so he injected guinea-pigs for a few weeks with an emulsion of the kidneys of rabbits; and he states that under these circumstances the serum of the guinea-pig so treated acquires such toxic properties that doses of 1 to  $2\frac{1}{2}$  c.c. per kilogramme not only cause albuminuria, but might bring about death from uræmia on the third or fifth day after the injection of this fortified serum into rabbits. These experiments, if confirmed, might not only throw an entirely new light on our conception of the action of renal poisons, but it is also conceivable that they might lead to the production of antitoxins useful for the treatment of renal disease. Lindemann sums up his observations by stating that he has never found the serum of normal guinea-pigs to cause any more serious symptom than a transitory albuminuria, and he quotes an experiment in which a rabbit received 8 c.c. of normal guinea-pig serum and yet presented no morbid symptoms during seven days. He then injected into this rabbit 8 c.c. of the serum of a guinea-pig which had been injected with the emulsion of rabbit's kidney. The rabbit that received this injection developed albuminuria a few hours afterward, and in two days complete suppression of urine occurred, causing the death of the animal in twenty-four hours afterward. Not only has Lindemann found that this serum is toxic, but he also states that it has a profound action on the structures of the kidney, and he describes necrosis and great disintegration of the epithelium of the convoluted tubules. The glomeruli, however, did not show any alteration. To this prepared serum of the guinea-pig he gives the name, following the terminology of Ehrlich, of nephrolytic serum, and he considers that the toxic substance is formed in the blood of the guinea-pig as a direct result of the processes of absorption of the injected kidney. It is impossible to criticise these observations here, but it is clear that if they should be substantiated—in other words, if it should be shown that the organism is capable of reacting in such a way after the injection of kidney substance that it produces in the blood-stream a substance capable of exerting a profound toxic action on kidney substance—our views as to the pathology of renal diseases might have to undergo great alterations. Remarkable as these experiments are, they resemble in many respects those previously described by Metchnikoff as regards the

production of the spermatotoxic substance, and those of Bordet and Ehrlich with reference to the production of hæmolysines.

### THE TREATMENT OF BRIGHT'S DISEASE.

The principles of the treatment of Bright's disease are, speaking broadly, to spare the kidneys as much as possible, because of the very prevalent view that owing to the damaged condition of the renal structures the excretory activity of the organ is very considerably impaired. The work that the kidney has to do can be diminished principally by giving a suitable diet and by promoting the activity of other excretory mechanisms, such as those of the skin and those of the bowel. In the dietetic treatment the main principle has usually been to cut down the nitrogenous ingesta as much as possible, and mainly for two reasons: first of all because the quantity of urea that is excreted in Bright's disease is below the normal, and the amount of urea in the blood and other fluids of the body generally is greatly above the normal; and, in the second place, owing to the presence of albumin in the urine, it is considered advisable to restrict the proteid diet. It was for these reasons that the treatment of Bright's disease by a milk diet was received with such favor, and doubtless in many cases this treatment has been very successful. The matter, however, is not as simple as it seems at first sight, since the proteid ingesta cannot be diminished below a certain quantity, as it is well known that even during starvation the excretion of nitrogen is still fairly free, and thus in the treatment of Bright's disease or of other kidney diseases we are on the horns of a dilemma: if sufficient proteid food is not given the proteid tissues will undergo disintegration, and, on the other hand, owing to the damaged condition of the kidney, it is very desirable to diminish the proteid ingesta to as great an extent as possible. Further, it is probable that in renal disease, especially when advanced and associated with great destruction of the kidney tissue, there is an increased disintegration of the proteid tissues of the body, as several observers have now shown that after experimental lesions of the kidney there is a greater loss of weight than during starvation. This increased proteid metabolism as a result of renal disease still further complicates the dietetic treatment of the condition. It is more especially in chronic Bright's disease that it is difficult to formulate rules for dietetic treatment, as in acute Bright's disease, owing to the very considerable suppression of the urinary functions which occurs during the height of the malady, it is essential to restrict the diet; and all physicians are agreed that in acute Bright's disease milk, and milk only, should be ordered, and that in the more severe

forms of the affection the quantities ordered should not exceed from one to two pints in the twenty-four hours. This small amount of milk can be ordered in such an acute disease, since the duration of the acute stage is short, and a few days may turn the scale one way or the other. In chronic Bright's disease the matter is very different, since there we have to deal not only with the lesion in the kidney, but also with the secondary results produced by this on the economy, leading to great wasting, anæmia, and cachexia. Some authorities would treat Bright's disease on the lines advocated by the late Sir George Johnson, by giving a copious milk diet for long periods at a time, as, for instance, six months, or even longer, this treatment being based on the view of giving the kidney as little work as possible, and in the hope that with the sparing of the kidney the lesion in it would subside, and that ultimately the body generally would benefit. On the other hand, more recent observers are in favor of treating the patient with a more liberal diet, with the idea that with the improvement in the general health, brought about by the liberal diet, the kidney lesion would undergo amelioration. The modern tendency is not to restrict the diet in cases of chronic Bright's disease to the same extent as was formerly the case. In the treatment of chronic Bright's disease by dieting it must be remembered that there is a considerable waste of the foodstuffs, owing to the fact that nausea, vomiting, and diarrhœa are all of them common symptoms of this form of Bright's disease. Further, owing to the presence of albuminuria, a considerable proportion of the proteids of the blood, and, therefore, indirectly of the food, passes off into the urine; and patients with chronic Bright's disease may pass as much as from 20 to 40 grammes of dry proteid in their urine per diem—quantities equivalent to the amounts present in one and two pints of milk respectively. Inasmuch as the minimum amount of proteid necessary for an adult is that contained in from three to four pints of milk—70 to 80 grammes—it is obvious that a restricted milk diet in chronic Bright's disease may supply a totally inadequate amount of proteid for the metabolic processes of the body; and, therefore, it is not surprising that many such patients do not improve on this diet. If the milk diet be increased to quantities sufficient to supply the necessary amount of proteid, bearing in mind the waste produced by losses from the alimentary canal and owing to the albuminuria, the large quantities required may produce other ill effects. These ill effects in a certain number of cases are confined to gastric disturbances, the large quantities of milk causing increased nausea or even vomiting; but in other cases, as shown by Romme,<sup>1</sup> the large quantities of milk prescribed tend to produce cardiac dilatation,

<sup>1</sup> *La Presse Médicale*, October, 1879.

apparently owing to the effect on the blood-pressure produced by the ingestion of large quantities of fluid. Many patients with chronic Bright's disease used formerly to be treated with quantities of milk of from five to ten pints per diem, although when these large quantities were given it was usually necessary to skim the milk. These large quantities of milk are probably not only harmful in the ways indicated above, but they are also unsuitable, owing to the fact that the quantity of proteid matter supplied is out of proportion to the amount of carbohydrate and fatty material, and really the diet is one tending to promote an excessive nitrogenous metabolism. Hale White, some years ago, pointed out that a milk diet, either in large or in small amounts, was not really suitable for the prolonged treatment of chronic Bright's disease; and these views of his have been substantiated by other observers, and more recently by Mills.<sup>1</sup> Milk is of value, therefore, mainly in the treatment of acute Bright's disease, and also in chronic Bright's disease temporarily, more especially during subacute exacerbations of the malady or when uræmic manifestations are marked. But it is probable that a prolonged milk diet is of no great value for the treatment of chronic Bright's disease, for the reasons mentioned above. In dieting a patient with chronic Bright's disease stress is usually laid on the amount of urea that is excreted per diem and on the amount of albumin present in the urine. A liberal diet tends to increase the albuminuria of renal disease just as it may increase physiological albuminuria; but the increase in the albuminuria produced in renal disease by a liberal diet is quite trivial in amount when compared to the increased amount of proteid given. Therefore, the mere fact that the albuminuria is slightly increased by the diet is not of itself a sufficient argument for restricting the diet. Observations on the quantity of urea excreted in renal disease have always to be corrected, as mentioned above, by the amount of albumin that is lost in the urine and by taking into consideration the presence or absence of vomiting and of diarrhœa. Although the quantities of urea excreted in Bright's disease may be far below the normal for a healthy adult, yet they do not necessarily point to the conclusion that the efficacy of the kidney as an excretory organ is greatly impaired. Thus, a patient passing some 15 grammes of urea a day, roughly speaking, half the normal quantity, may really be excreting all the urea that is supplied to the kidney, owing partly to the diminished appetite, partly to the nausea and vomiting, and partly to the loss of albumin in the urine; so that here again the dietetic treatment should not be determined entirely by the mere amount of urea present. If an increased diet leads to a diminution in the quantity of urea passed,

<sup>1</sup> Medical Record, 1899.

together with an increase in the amount of albumin, it is probably not beneficial; and in some cases, in addition to these ill effects, uræmic symptoms may develop. On the other hand, in a very large number of cases of chronic Bright's disease an increase in the diet will be followed by a considerable improvement in the patient's general condition, his strength and color improving, although no profound alteration may take place in the composition of the urine. Mills is of the opinion that even red meat is permissible once a day, and that chicken, eggs, and fish may all be used. All observers are agreed that alcohol is harmful.

In the treatment of chronic Bright's disease care must always be taken to make a differential diagnosis between chronic Bright's disease and the waxy kidney, inasmuch as these two conditions may resemble one another clinically. In amyloid disease of the kidney, however, the efficiency of the organ as a filter is not necessarily greatly impaired, and such patients require a very much more liberal diet than cases of ordinary chronic Bright's disease. In waxy kidney not only is a liberal diet required, containing an abundance of proteid food, but in addition stimulants are frequently advisable, and the dietetic treatment of the condition must be directed rather to that of the original malady which is causing the waxy disease than determined solely by the condition of the kidneys. If the disease is very advanced and uræmic complications are present, then the malady requires a similar dietetic treatment to that of Bright's disease. In the granular kidney the great object is to prevent the evil results produced by high tension. Little can be done to influence the renal lesion itself. In many cases this malady has been brought about by excessive indulgence in the pleasures of the table, and there can be no doubt that it is most advisable to restrict the diet in such cases, as it is well known that large and copious meals produce very profound effects on the general blood-pressure. As mentioned above, Romme has shown that the ingestion of large quantities of fluids in this malady may be harmful and may tend to develop cardiac complications. Patients suffering from granular kidney may live in comfort for many years if all precautions are taken to avoid strain and if a simple diet be given, so as to prevent as far as possible any tendency to raising the blood-pressure.

### RENAL TUMORS.

The main interest of renal tumors at the present day is with reference to their pathology, owing to the confusion that has existed for many years as to the nature and classification of renal growths. This confusion arises largely from the fact that the elements found in renal tumors are often of very diverse natures, and thus the same growths

have been described by some as carcinomata and by others as sarcomata. The interest, however, is not entirely limited to the pathological side, inasmuch as the successful treatment of renal tumors depends to a very great extent on their nature. One variety of malignant disease of the kidney, namely, that beginning in the adrenal rests, is peculiarly amenable to early surgical interference. A thoroughly satisfactory classification of the varieties of renal tumors probably does not exist, but one of the latest, advocated by Kelynack,<sup>1</sup> is at any rate a convenient one.

He divides the tumors into :

1. True renal growths.
2. Pelvic growths.
3. Hilum growths.
4. Capsular growths.
5. Growths arising from adrenal inclusions.
6. Adrenal growths.
7. Perirenal growths.

Groups 6 and 7 cannot, strictly speaking, be included among kidney tumors, although they may secondarily involve the kidney. With reference to true renal growths, Kelynack considers that these may begin in the connective tissue of the kidney or else in the epithelium of the kidney. Those beginning in the connective tissue of the kidney are further divisible into benign, such as fibroma, and the malignant, such as sarcoma. Those originating in the renal epithelium are, if benign, adenomata ; if malignant, carcinomata, or, as it has been called by many, a malignant adenoma. Sarcomata, adenomata, and carcinomata are unquestionably the most common forms of renal tumors. Carcinomata of the kidney are usually held to begin in the epithelium of the tubules, but recently a case has been described by Abram as one of carcinoma of the kidney arising in the glomeruli, and this is of sufficient interest to be quoted in some detail.<sup>2</sup> The patient came under observation on account of anæmia and emaciation, with enlarged glands in the groin, axilla, and submaxillary regions, in addition to which there were two tumors on the anterior surface of the sternum. During the course of his illness tumors developed on the ribs, the liver became enlarged and nodular, and the patient died after ten months' illness. A number of growths were found at the post-mortem on the anterior and posterior surfaces of the sternum, and a large growth was also found involving the vertebral column. The liver contained many nodules of growth, and the kidneys were large and showed, macroscopically, one or two small nodules of growth. The growths from the different parts of the body, on microscopical examination, presented the same

<sup>1</sup> Edinburgh Medical Journal, 1899.

<sup>2</sup> Journal of Pathology, 1900, vol. vi.

structure, and the tumor was found to be epithelial in nature. The tumor tissue consisted of slender cells packed in irregular alveoli, the central portion showing many necrotic cells, and in places the stroma had undergone myxomatous degeneration. In the case of the tumors involving the bones only the periosteal surface of the bone was affected, the medullary substance being normal. The growths in the liver resembled in structure those of the bones. The kidneys, in addition to slight sclerosis of the cortex, showed that the glomeruli were affected in a remarkable manner. The glomeruli were unduly prominent to the naked eye, and this prominence was dependent on a thick layer of epithelium lining the parietal layer of Bowman's capsule. The epithelial lining of the capsule consisted of several layers of slender columnar cells with oval nuclei. In the majority of cases the vascular tuft and its epithelial covering were normal. In some cases the proliferating epithelium completely filled the capsule, and in places the growth penetrated the basement membrane and infiltrated the surrounding tissue, and here and there the epithelium of the renal tubules close to the glomeruli was replaced by that of the growth. The small nodules of growth which were seen in the kidney were found to consist of masses of cells with a considerable amount of stroma in which some bundles of fibres resembling muscular fibres were present. Abram remarks that the occurrence of a malignant epithelial tumor in a youth, aged sixteen years, is very unusual, and that he has only been able to find two cases on record in which the peculiar condition of the kidney found in his own case was present. These are one by Hildebrand, of a small-celled carcinoma in a child, aged five years, which was considered to arise in the glomeruli; and another of Sharkey,<sup>1</sup> in a woman, aged twenty-eight years, which closely resembled Abram's case in the fact that the kidney showed that the basement membrane of the capsules was sharply defined and the capillaries were healthy, but from the internal surface of the basement membrane there arose a deeply stained layer of cells having a clear columnar arrangement. Abram discusses whether the condition in the glomeruli in his case was congenital or was dependent on carcinoma. He considers that although the widespread affection of the glomeruli was in favor of the congenital theory, the fact that the cellular mass consisted of more than one layer is strongly in favor of a new formation, as the epithelium of the primitive renal tubule in man and in animals consists of a single layer of cells. For this reason he considers that the change in the glomeruli was of the nature of a new growth, and he considers that it was a primary growth of the kidney, notwithstanding the fact that the

<sup>1</sup> Transactions of the Pathological Society, London, 1882.



growths in other parts of the body were more developed. Since the growth was limited to the parietal layer of Bowman's chamber, Abram considers that it was primary; if the growth had been secondary it would have involved the vascular tufts as well as the peripheral part of the capsules, and he considers, finally, that the growth was one of primary carcinoma of the kidney arising in the glomeruli and perhaps associated with a persistence of the epithelium of the primitive renal tubule. The fact that fibres resembling muscular fibres were also found in Abram's case affords some support to the view that a congenital anomaly played some part in the development of the condition. If these views are accepted, malignant renal growths must be held to arise not only from the epithelium of the renal tubules, but also from the epithelium lining the glomerular chamber.

Pelvic growths or growths involving the pelvis of the kidney are, as Kelynack points out, generally of the nature of a malignant papilloma, sometimes epithelioma. Hilum growths and capsular growths are generally sarcomata. A very interesting form of growth is that arising from congenital anomalies, and a considerable number of such cases have been described of recent years under a variety of names, owing to the great varieties in the tissue elements present. These are the tumors which are especially liable to contain muscular fibres in addition to cells arranged more or less in the form of an adenoma. They have been described as carcinomata, sarcomata, endotheliomata, rhabdomyoma, and more recently as embryonal adenosarcoma. These mixed renal tumors usually occur in the young, and are not infrequently congenital and, as pointed out by Herzog and Lewis,<sup>1</sup> they not uncommonly reach a very large size, and the initial symptoms produced are frequently not renal, but simply dependent on the mere size of the tumor; so that it is not an uncommon event for the child to come under observation owing to the mere increase in the size of the abdomen. Renal tumors dependent upon congenital anomalies, although very characteristic of the renal growths seen in infants and in children, are not limited to the young, and may occur in the adult or even in the elderly. When this is the case their structure resembles more closely that of the suprarenal, and the tumor mass is not so liable to contain striated muscular fibres and to be so heterologous as in the case of the congenital tumors or those occurring in the first years of life. McArthur and Esendrath<sup>2</sup> described a tumor of this character under the title of hypernephroma of the kidney in a man, aged forty-seven years. This tumor was apparently of adrenal origin, and was distinctly encapsuled and could be

<sup>1</sup> American Journal of the Medical Sciences, June, 1900.

<sup>2</sup> Philadelphia Medical Journal, 1899.

separated from the renal substance, and it presented the yellow appearance which is so frequently seen in these tumors and which has led to some of them being described as lipomata. In a case of this kind which fell under the observation of the writer, and where ultimately the kidney was successfully removed, the first symptom drawing attention to the condition was hæmaturia, and this occurred seven years before the nephrectomy. In the congenital form of renal tumor, which may perhaps be called embryonal renal adenosarcoma—a name applied to it by Herzog and Lewis—microscopical examination showed that the tumor was composed of two different kinds of tissue—epithelial and connective tissue—and the authors draw attention to the fact that in some places the epithelial element preponderated, and in others the connective tissue; and they formed the opinion that the two kinds of tissue had originated quite separately. The epithelial elements were arranged in the form of alveolar nests surrounded by connective tissue, and in places the cells were arranged in such a manner as to surround tubular gland spaces. Herzog and Lewis consider that the cells forming the nests closely resemble the cells lining the tubules which empty into the Wolffian ducts in the human embryo. The connective-tissue areas of the tumor show in small amount striated muscular fibres very similar in structure to those of the normal, but in much larger amount muscular fibre which approximates to the embryonic type, with large, oval nuclei lying inside the sarcoplasm, and with distinct but very fine striation. Microscopical examination of these tumors shows that both the epithelial and the connective tissue elements approach closely to the embryonic types, and Herzog and Lewis consider that they owe their origin to an anomaly in the developmental process, so that the nephrotome is not separated in the normal manner, but includes a portion of the myotome; and, further, that the separation may take place in such a manner that only a portion of the myotome proper is cut off, or in addition a portion of the sclerotome. This view affords a ready explanation of the fact that these embryonic tumors contain such mixed elements as striated muscle, cartilage, connective tissue, and epithelium.

It would seem, therefore, that two varieties of tumor arising as a result of congenital or developmental anomalies may be found in the kidney. First, the tumor arising in an adrenal rest, which may have simply an adenomatous structure and run a more or less benign course; in other cases a tumor of similar origin may partake more of the nature of a sarcoma or carcinoma and run a malignant course. Second, the embryonic renal adenosarcoma which arises also as a result of an earlier developmental anomaly, owing to the portion of the mesoblast which develops ultimately into the permanent kidney not being separated off from the myotome in the normal manner.

Primary growths in the suprarenal bodies may during life be mistaken for renal tumors, although they are perfectly distinct from these. Morris<sup>1</sup> classifies such tumors into three groups :

1. Where the increase in size is due to a simple glandular proliferation.
2. Where an adenoma, usually large, is produced.
3. Where the growth develops, running a malignant course clinically, and has been variously described as carcinoma or sarcoma.

Morris considers that these tumors can frequently be diagnosed from renal tumors by the fact that the kidney can be felt displaced and prominent on the surface of the tumor mass, and also owing to the fact that the mobility of the tumor is frequently considerable and greater than that which one is accustomed to find with the ordinary renal tumor. These tumors generally grow rapidly, and they tend to form secondary deposits, more especially in the skin and in the liver. The urine remains normal, but marked emaciation and loss of strength occur, and in some cases pigmentation of the skin. Morris has also described in exceptional cases a marked and rapid growth of hair over the body. These tumors are, however, mainly of pathological interest.

### RELATION OF BRIGHT'S DISEASE TO SYPHILIS.

Nephritis and Bright's disease are most frequently seen as sequelæ or complications of acute specific diseases, and Bright's disease is, as is well known, most prone to occur during convalescence from these specific affections. Although all acute specific diseases may be followed by these renal complications, it is thoroughly well recognized that scarlet fever is the one where these sequelæ are most likely to develop. Not only are acute infections liable to be followed by these renal complications, but the same is true of chronic infections. Syphilis, however, although a specific infective disease, is not so universally recognized as a factor in the production of renal disease, notwithstanding that cases are seen from time to time where the occurrence of nephritis during the incidence or convalescence of syphilis suggests a close relationship between the two diseases. The relationship of nephritis, and even of Bright's disease, to syphilis resembles to a certain extent the relationship of transverse myelitis to the same malady. Delamare<sup>2</sup> has recently returned to the consideration of this subject. Syphilis may lead to renal complications, both during its secondary and during its tertiary stage ; and tertiary affections of the kidney were recognized long before it was admitted that secondary syphilis was liable to be followed by renal complications.

<sup>1</sup> British Medical Journal, 1899.

<sup>2</sup> Gazette des Hôpitaux, May, 1900.

The most frequent tertiary lesion of the kidney is amyloid degeneration. Occasionally gummata are found, and acute and subacute nephritis have also been described. Some authorities consider that chronic interstitial nephritis and granular kidney may also be looked upon in some cases as a tertiary syphilitic lesion. The combination of gummata in the kidney with extensive amyloid degeneration is by no means an infrequent one, and usually in such cases there is evidence of amyloid degeneration in other organs, as, for instance, the liver, the bowel, and the spleen. Although the presence of gummata in the kidney cannot be diagnosed, the waxy degeneration associated with tertiary syphilis is peculiarly apt to be looked upon clinically as chronic Bright's disease; and this is an unfortunate error, since many such cases, even where the amyloid degeneration is extensive, undergo very considerable improvement if their true nature be recognized. Amyloid degeneration is peculiarly apt to be erroneously diagnosed as Bright's disease if such a diagnosis is hurriedly made from the mere presence of albuminuria or even albuminuria associated with dropsy. Although in some stages of the amyloid kidney a diet similar to that prescribed in Bright's disease may be advantageous, as, for instance, where amyloid disease has advanced to such an extent as to lead to the presence of uræmic complications, in the large proportion of cases of amyloid disease a much more liberal diet is required. In other words, such patients, unless uræmic complications are present or imminent, should not be treated with a rigid milk diet. Where the amyloid disease is the sequel of syphilitic infection, antisyphilitic remedies are also frequently of great value, and, therefore, for these two reasons the recognition of the syphilitic origin of the condition is a most important practical point. Where granular kidney is seen as a result of syphilitic infection the nature of the lesion is such that the antisyphilitic treatment does not produce the beneficial effects that are seen in waxy disease. Where renal disease complicates secondary syphilis the nephritis is usually acute or subacute, and according to Delamare the chronic form is rare. There are considerable resemblances between the acute nephritis of syphilis and that complicating scarlet fever, and some cases of nephritis may be seen in secondary syphilis, apparently as a result of exposure to cold. Cases of acute and subacute nephritis dependent on syphilitic infection are difficult to diagnose, and Delamare points out that one of the characteristic features of the condition is that a milk diet produces very little improvement, whereas the administration of antisyphilitic remedies is immediately followed by striking improvement. The relation of nephritis to syphilis has been differently explained by different observers. At one time the view was held that the nephritis was dependent on the mercury administered in the treatment of the disease. It is, of course,

true that the heavy metals, mercury and lead, like the mineral acids, are capable of producing nephritis if they are given in sufficient doses for prolonged periods ; and perhaps in the days when syphilis was injudiciously treated by the administration of huge doses of mercury this result may sometimes have been produced ; but with the modern treatment of syphilis the view cannot be accepted that the nephritis complicating it is dependent on an injurious action of mercury. This is a matter of some importance, not only with reference to syphilis, but also to the employment of mercurial salts generally. Many clinicians are chary of prescribing mercury, even in the form of a purge, to patients suffering from renal disease. The danger of mercury in renal disease has probably been overrated. Not only are the salts of mercury often valuable purges, but it is possible that some of the salts of mercury may be beneficial from their action as slight diuretics. Not only can we not admit that mercury is the cause of the nephritis that is seen complicating syphilis, but the administration of mercury in such cases is often followed by most striking improvement in the condition. Syphilis may act as a direct exciting cause of nephritis or as a predisposing cause, in the latter case the renal complication being dependent on some other factor, the efficacy of which depends on the presence of the syphilitic cachexia. The renal lesions in syphilis are not restricted to the acquired disease ; they may often be found in cases of hereditary syphilis, and in such cases gummata in the cortex and in the medulla of the kidney are not uncommon, and, in addition to this, contracted kidneys, both white and red, have been described. Delamare considers that during the acute stage of the nephritis complicating syphilis a milk diet is useful, as it is in other forms of acute nephritis ; but it is essential to prescribe antisyphilitic remedies, both mercurial salts and the iodides, and very often the administration of these substances produces a striking improvement in cases where a milk diet by itself has failed. The main point of interest to clinicians is, that where nephritis occurs in adults and there is a possibility of its being dependent either on secondary or tertiary syphilitic infection, that cautious treatment with antisyphilitic remedies should be adopted, and that mercury should not be withheld from the dread of the toxic action of this substance where nephritis is present.

### DEVELOPMENT OF MALPIGHIAN BODIES.

Herring,<sup>1</sup> in an elaborate paper on the development of the Malpighian bodies in the human kidney, adduces a number of facts which are of considerable interest from a pathological point of view. He shows that

<sup>1</sup> *Journal of Pathology*, 1900, No. 4.

in the human subject the kidney arises from two distinct structures, one a mass of cells of mesoblastic origin, in close relation to the Wolffian body, and secondly from the ureter. The ureter develops as an outgrowth from the Wolffian duct, and grows forward into the mass of cells mentioned above, and known as the kidney blastema. The Malpighian bodies, convoluted tubules, Henley's loops, the junctional tubules, connective-tissue framework, and the capsule of the organ are formed from the kidney blastema; while the ureter, pelvis, calices, and collecting tubules are formed from the ureter. Malpighian bodies and their tubules begin to appear at the end of the second month of foetal life, and new Malpighian bodies are formed as late as the end of the eighth month. In the foetal kidney Malpighian bodies seem to be more abundant in relation to the convoluted tubules than later, and the convoluted tubules, which in the adult make up the bulk of the cortex, are almost absent at the fourth month. The glomerulus, Herring considers, is formed not by an invagination, but by a thickening of the epithelium, and the capillaries of the glomerulus are developed *in situ*, each Malpighian body with its tubule having arisen as a solid mass of cells which later acquires a lumen and takes the shape of an S, the lower limb of the S becoming the Malpighian and the upper and middle limbs forming the convoluted tubules. The cells in Bowman's capsule may be divided into those lining the capsule and those covering the glomerulus. Herring shows that the cells covering the glomerulus are more highly differentiated than those lining the capsule. Those covering the glomerulus are at one stage very similar in character to those lining the tubules, and are columnar or cubical in shape, whereas those lining the capsule are flatter, and are developed from cells closely allied to those which form the lining of the general peritoneal cavity, and, as Herring points out, in Bowman's capsule they have no further function than to form the wall of a cavity, which is, after all, only a portion of the body cavity. In disease the differentiation between these two kinds of cells is seen by the different way in which they react to morbid processes, the cells lining the capsule reacting much in the same way as those in other serous cavities, whereas those covering the glomerular tuft are often affected in a special manner. The selective action of morbid processes is also further shown by the striking manner in which nephritis and Bright's disease produce their greatest effects on the mesoblastic structures of the Malpighian bodies and the convoluted tubules. The epiblastic structures of the kidney, forming as they do the pyramids—*i. e.*, the collecting tubules—undergo but little change in these conditions. The different actions of the morbid process on the different cell elements in the glomerular chamber are well shown by the fact that in disease the cells covering the capillary tufts, like the

cells lining the convoluted tubules, are prone to undergo degeneration and necrosis, and are frequently shed *en masse*. On the other hand, the cells lining the chamber, which are endothelial in character, tend to proliferate and ultimately to form organized connective tissue.

### THE INTERNAL SECRETION OF THE KIDNEYS AND THE NATURE OF URÆMIA.

The striking results that were obtained in the physiology of the thyroid gland by Schiff and Horsley, establishing on a firm basis the existence of internal secretions and proving the correctness of an old idea of Brown-Séquard, not only threw a new light on the pathology of the diseases of the thyroid, but also led pathologists to think that other glands might be provided in the same way with internal secretions. Brown-Séquard himself was of the opinion that many glands in the body possessed these internal secretions in addition to external secretions. This is notably the case with the liver, as the glycogenic function of this organ can certainly be described as an internal secretion, inasmuch as the formation of sugar by the liver is on all fours with the formation of a colloid material by the thyroid. Brown-Séquard was of the opinion that the kidney also was provided with an internal secretion, and he considered that the abrogation of this internal secretion was the real cause of the phenomena of uræmia. He advanced this view in 1889, and from that time to the present this conception of the kidney being provided with an internal secretion is one that has been constantly revived, and has influenced not only the views as to the nature of uræmia, but also the treatment of this condition. Brown-Séquard himself suggested that kidney extracts might be used with advantage in the treatment of uræmia. Chatin and Guinard<sup>1</sup> return to this question, and they point out that the arguments which have been adduced in favor of the existence of an internal renal secretion are based on three groups of facts: First, certain phenomena observed clinically; second, the experimental results of nephrectomy, and, thirdly, the results of treatment with kidney extracts. From the clinical side no doubt there are some facts which at first sight lend considerable support to the view that uræmia is dependent on the cessation of an internal renal secretion. It has been established for many years that calculus anuria may exist for a week to ten days without the production of any of the ordinary symptoms characteristic of uræmia. This was observed by Sir William Roberts<sup>2</sup> in 1872, and Merkle, in 1881,

<sup>1</sup> De la Sécrétion interne du rein., Archiv de Méd. Exp., 1900, No. 2.

<sup>2</sup> Urinary and Renal Diseases, 2d edition, 1872.

collected a large number of these cases. In many of these cases of calculous suppression the patient not only lives for a week or ten days without presenting any symptoms of uræmia, but may at the end of as long a period as eight days suddenly recover completely, either spontaneously as a result of the passing of the calculus or as a result of surgical interference, and this recovery may take place without the production of any severe symptoms. The only phenomena that are produced by the long duration of the complete suppression of urine are a slowing of the pulse, a lowering of the body temperature, and contraction of the pupil. Fowler,<sup>1</sup> in 1899, also collected a large number of such cases, amounting to ninety-three, and only nineteen of them presented symptoms of uræmia. The striking fact that calculous anuria may exist for these long periods without the production of any of the ordinary symptoms of uræmia is one that has struck every clinician, and no doubt at first sight the contrast offered between these cases and those of acute uræmia supervening, for instance, in nephritis, affords strong presumptive evidence of the existence of an internal secretion. In cases of nephritis and other destructive diseases of the kidney it has usually been held that uræmic phenomena of great violence become developed generally within three days after the onset of the suppression. The explanation that Brown-Séquard gave of these facts is very plausible, namely, that uræmia was not the result of the suppression of the renal excretion only, but that it only occurred when the suppression of the renal excretion was accompanied by the arrest of the hypothetical internal renal secretion. Brown-Séquard adduced further evidence in support of this view by performing double nephrectomy on rabbits and guinea-pigs and then injecting into these animals renal extract; and he stated that under these circumstances the animals receiving the extract lived longer than the others. Meyer,<sup>2</sup> in 1894, repeated these observations, using a glycerin extract of the kidney of the dog, and experimenting both on dogs and on rabbits. He found that if double nephrectomy was performed on dogs, after some thirty-six hours Cheyne-Stokes respiration became marked. He injected into these animals 20 c.c. of his renal extract, and found that, although death was not prevented, the Cheyne-Stokes respiration temporarily disappeared. He performed another series of experiments in which, after double nephrectomy, he bled the animals to the extent of 60 c.c. and replaced this by 6 c.c. of defibrinated blood from healthy animals; and here also he noticed that some of the uræmic phenomena, such as the Cheyne-Stokes respiration, underwent improvement. In the third series of animals he performed a similar experiment, but, instead of injecting blood of the general cir-

<sup>1</sup> Medical Record, New York, 1899.

<sup>2</sup> Archiv f. Physiologie, 1894.



culatation, he injected the defibrinated blood obtained from the renal vein of a healthy dog. He states that the same favorable results were obtained, but lasted longer. Meyer concludes from these observations that the blood of the renal veins contains some material elaborated by the activity of the kidney and capable of exercising a beneficial influence in the toxic condition that supervenes after double nephrectomy. Vitzow performed double nephrectomy in dogs and rabbits, and claims that such animals after the injection of blood from the renal vein of healthy animals live longer than control animals. These observations have been repeated by the Italian observers Ajello and Parascandolo,<sup>1</sup> who showed that the injection of renal extract after double nephrectomy prolonged the duration of life. Tigerstedt and Bergman<sup>2</sup> considered that the hypothetical internal secretion of the kidney had an action on the circulation in that they stated that the extracts of the cortical substance of the kidney had a vasoconstrictor action on the bloodvessels. This observation, however, has been contradicted by Levandowski, who failed to obtain any results from the injection of renal extracts on the circulation, and considered, inasmuch as this was the only evidence in favor of an internal renal secretion, that such a secretion did not exist. The arguments that have been adduced in favor of an internal renal secretion from therapeutical observations are not very convincing. A number of cases have been described of Bright's disease and of uræmia complicating other renal affections in the human subject which have been said to undergo a transitory improvement as a result of the subcutaneous injection of renal extracts. Dieulafoy, Tessier, and Fränkel have all recorded cases in which the injection of this material has been followed by a prompt diuresis, with an improvement in the uræmic condition. More recently De Lignerolles<sup>3</sup> has used, instead of glycerin extracts of kidney substance, the serum obtained from the renal vein of goats. This author has used this material in doses of 20 c.c. in the treatment of four cases of uræmia. In one case of uræmic coma the condition was not in any way influenced by the treatment; but the other three cases were stated to have undergone improvement, and the improvement showed itself not only in the general condition of the patient, but also in a diminution of the toxicity of the urine, and also in a progressive diminution of the albuminuria. Chatin and Guinard consider that there is definite evidence clinically of the beneficial results produced by this treatment, notwithstanding that they acknowledge the numerous sources of error owing to the way in which uræmia as a result of other treatment will often undergo very great and sudden improvement.

<sup>1</sup> *Lo Sperimentale*, Anno 49, fasc. iv.

<sup>2</sup> *Archiv f. Physiologie*, 1898.

<sup>3</sup> *Thèse de Lyon*, 1898.

In the opinion of the writer the arguments founded in favor of the existence of an internal renal secretion based on the phenomena observed in calculous anuria are not so convincing as they at first sight seem. There is definite evidence that in the human subject the clinical picture of latent uræmia associated with calculous suppression, and so characteristic of it, is not really limited to this condition; and precisely similar phenomena may be seen in cases where the entire kidney is destroyed, as in the case recorded by Bradford and Lawrence,<sup>1</sup> where, as a result of thrombosis of the renal arteries on both sides, the entire cortex of both kidneys was necrotic, and where the patient survived for a week without secreting any urine, presenting the clinical picture of calculous suppression. Such a case affords strong evidence against the theory that uræmia is dependent on the cessation of an internal secretion produced by the kidney, since if this were so, in such a case an acute uræmia similar to that seen in other renal affections should have been produced. It would seem as if the sudden cessation of the renal excretion, whether as a result of calculous suppression or as a result of obstruction of the circulation through the kidney, produces in both cases the phenomena of latent uræmia, and not those of acute uræmia. This may be interpreted in one of two ways: either the uræmic phenomena differ according to the dose of poison, or else uræmia is not dependent on the retention of any normal constituent of the urine, but rather on the formation of abnormal substances as a result of the disintegration of the tissues, which is such a characteristic phenomenon of renal disease.

The treatment of uræmia by kidney extracts cannot offer such a prospect of success as is seen in the treatment of such a condition as myxædema by thyroid extract, since, whatever other functions the kidney may have, it is impossible to conceive that life can be maintained when its excretory function is seriously abrogated unless the excretion of the normal urinary constituents can be effected by other channels, such as the skin and the bowels.

**The Influence of Diet on the Formation of Uric Acid.** The formation and excretion of uric acid plays a large part not only in the pathology of gout, but also in that of renal diseases, and more especially in the formation of calculi. Uric acid may also play a part in the production of certain diseases of the kidney, as, for instance, granular kidney; and, on the other hand, diseases of the kidney, such as the granular kidney and certain varieties of Bright's disease, and perhaps some functional derangements of the kidney, may play a part in the etiology and in the nature of gout. All problems, therefore, associated with the seat of formation of uric acid and also with its chemical

<sup>1</sup> Journal of Pathology, 1899.

origin are of importance to the physician, to the pathologist, and to the therapist.

Both the seat of formation of uric acid and its mode of origin are open to some doubt, although from a physiological stand-point most observers are agreed that the liver is the organ which is, either mainly or exclusively, concerned with its formation. In recent years the older view that the kidney is the seat of origin of uric acid has been revived; but at any rate, from an experimental stand-point, the evidence in favor of this view is extremely scanty, whereas that which locates the seat of its formation in the liver rests on a firm experimental basis, in that removal of the liver is followed by a diminution of the amount of the uric acid excreted in the urine. The only experimental observation which in any way confirms the view that uric acid may be formed in the kidney is the old observation of Garrod's, that the blood of birds contains urea, and, therefore, the suggestion has been made that the kidney of birds converts urea into uric acid. It would be very desirable for observations to be made on the results following extirpation of kidneys in birds to settle this question; but we know that destruction of the bird's kidney by the injection of chromic acid is followed by the deposition of uric acid in the tissues. The only other evidence available supporting the view that uric acid is formed in the kidney is the fact that the activity of the renal protoplasm is capable of synthesizing benzoic acid with glycerin, so as to form hippuric acid. There the matter rests at the present day, and it cannot be said that human pathology affords any very strong evidence in favor of the view of the kidney being the seat of formation of uric acid.

As regards the mode of its origin, various views have been held in the past, but at the present day it is generally recognized that the uric acid and other such bodies in the urine, to which the general term *alloxur* bodies has been applied, have a double origin, a certain proportion of them arising from the metabolism of the *alloxur*-containing substances in the food, and the other being derived from the metabolism of the tissues of the body. It is obvious that the pathology of gout and the pathology of renal calculus must, in part at any rate, be dependent on the nature of the metabolism of these *alloxur* bodies, both those of the food and that of the tissues. The pathology of these two diseases, however, may not be restricted to disordered nutritive processes influencing the amount or the character of this metabolism, as it is possible that the chemical pathology of these two diseases may be associated more with the question of maintaining the *alloxur* bodies, and especially the uric acid, in solution in the blood and in the urine rather than with questions influencing the amount of these substances actually produced. Thus it is notorious that the deposition of uric acid from

the urine, with the formation of stones or gravel, is often associated rather with the percentage amounts of other saline ingredients present in the urine than with the actual percentage of uric acid present. Dilute urines often deposit uric acid with greater facility and greater readiness than concentrated urines, although the actual percentage of uric acid present may be far higher in the latter case than in the former. In the case of gout the pathologist has to deal with an excess of uric acid, and perhaps other alloxur bodies, in the blood. In the case of renal calculus and renal gravel he has to deal either with the excess of the same substances in the urine or with a premature deposition of these bodies in the urinary passages as a result of other anomalies of the urinary secretion, such as a low percentage of salts or a high grade of acidity.

The treatment of urinary calculus and of gravel is almost entirely dependent on a correct knowledge of the metabolism of these alloxur bodies and with the nature of the means by which uric acid is kept in solution in the urine.

The formation of uric acid has long been correlated with diet, and more especially with a meat diet. Diet alone, however, will not afford a sufficient explanation for the formation of uric acid, as is well seen from the fact that many carnivorous animals excrete little or no uric acid in their urine, and that, therefore, in organisms such as the human subject, where uric acid is a constant constituent of the urine, its presence there cannot be dependent entirely on diet. This is also seen from the fact that certain quantities of uric acid are also present in urine in the human subject during starvation. The amount of uric acid, however, in human urine is greatly influenced by the diet, as is shown by the notable increase that occurs after each meal. Some observers have thought that even this increase, closely related as it is with the absorption of food, is really dependent not on the actual food substances ingested, but on the physiological processes concerned with their absorption, and the view was at one time advanced that the increased excretion of uric acid seen after meals was dependent on the disintegration of the large number of leucocytes which are concerned with the process of absorption. This view arose from the fact that the excretion of uric acid was found to be greatly increased in certain diseases in which there was increased blood destruction or increased formation of white corpuscles. The two notable instances of this are pernicious anæmia, where there is great destruction of red blood-corpuscles, and leucocythæmia, where there is a large increase in the number of white corpuscles. It is, however, clearly established now that not only is there an increase in uric-acid excretion after meals, but that this increased excretion is especially marked with certain articles of diet; and a very

large number of observers have confirmed the original views of Habaczinski, who correlated the production of uric acid with the quantity of nuclein bases present in the food. The most complete work on the relation of the alloxur bodies in the urine to the food is that of Burian and Sehur,<sup>1</sup> and this research is one of considerable importance to the practitioner. These observers show that with an ordinary diet the alloxur bodies in the urine may be divided into two groups, to which they give the name of endogenous and exogenous respectively. The exogenous are derived from the alloxur bodies that are present in the food. The endogenous, on the other hand, are independent of the nature, and, what is still more important, the amount of the food, and vary for each individual, but at the same time are constant in amount for the same individual. This is a matter of considerable importance, at any rate in the pathology of such diseases as gravel and gout, as it is clear that a new light would be thrown on the nature of these diseases if it could be clearly established that in certain individuals the endogenous formation of these bodies was different to that of the normal individual.

In order to estimate the endogenous urinary alloxuric bodies the quantity of these bodies excreted during starvation may be determined. But this is not perfectly satisfactory, because in starvation the metabolism of the body is obviously altered, and a more satisfactory method is to feed the individual, as these observers have done, on alloxur-free diet, keeping the total amount of nitrogen given the same as under other conditions when alloxur bodies were allowed in the food.

As a first step in these observations the authors investigated the quantities of alloxur bodies present in various foodstuffs. They found that milk and eggs, rice, white bread, potatoes, and certain vegetables, such as ordinary salads and cauliflowers, contain practically no alloxur basis. Having determined this point, they then conducted a series of observations, divided into four periods. In the first a diet was given containing considerable quantities of meat, in which large quantities of alloxur bases, more especially in the form of hypoxanthine, are present. In the second period the meat was eliminated from the diet and the nitrogenous equilibrium maintained by giving quantities of milk and eggs. In the third period the same diet as in the second period was given, but cut down to one-half; but rice was added in sufficient quantity to afford a proper number of heat units. In the fourth period a strictly vegetable diet was given, but containing the same amount of nitrogen as in the third period. The nitrogenous excreta in these four periods were then investigated, and the quantities of uric acid and other

<sup>1</sup> Arch. f. de ges. Physiologie, Bd. lxxx.

alloxur bases in the urine determined. In the first two periods the total amount of nitrogen excreted was approximately equal, but the alloxuric nitrogen in the first period was considerably greater than that excreted in the second. This is, of course, what would be expected under the circumstances. It is a comparison of the second, third, and fourth periods, however, that yields the most interesting and important results from a practical point of view. In the second period, although the total nitrogen excreted was practically equal to that seen in the first period, the amount of alloxur bases in the urine was greatly diminished. The contrast of period two with period three yielded still more interesting results; although the total nitrogen excreted was nearly halved by halving the diet and substituting rice, the alloxuric excretion of period three was the same as that of period two. This was also the case in period four, where a vegetable diet was given.

Since the excretion of alloxuric bodies in periods two, three, and four remained constant, notwithstanding the great alterations in the composition and in the quantity of the foods administered, the quantities of alloxuric bodies excreted must represent the endogenous formation. It is a matter of considerable importance to the physician and the therapist that with a diet of milk and eggs sufficient to maintain nitrogenous equilibrium and to produce an excretion of nitrogen equal to that seen on a full flesh diet, the alloxuric excretion should be as small as that seen with a liberal carbohydrate diet or that seen with a strictly vegetable diet; and it is clear that these results would have a considerable influence on our views of the treatment of gout, gravel, and other maladies associated with uric acid. Not only is the excretion of the alloxur bodies fairly constant with these three different diets, but the excretion of uric acid itself is also very constant, and the quantities of uric acid excreted with the liberal milk and egg diet (period two), with the diet in period three (consisting largely of rice), and with the strictly vegetable diet in period four, are practically equal.

The quantities of alloxuric bodies excreted by the same individual with these several diets are not only equal, but they are also constant, and a repetition of the experiment on the same individual some six months afterward yielded the same results; and, therefore, we may conclude in the case of any given individual, provided his diet does not contain variable quantities of alloxur bodies, that his excretion of these substances in the urine will remain fairly constant.

The actual amount of alloxuric nitrogen excreted by a given individual with a more or less alloxur-free diet has been variously estimated by different observers. Burian and Sehur estimated it at about 0.2 grammes of nitrogen per diem. The authors conclude from their experiments that the following laws can be formulated: That the nitrog-

enous urinary alloxuric bodies can be directly determined by giving a diet consisting of eggs and milk sufficient to fulfil the requirements of nourishment; and, second, that in the same individual under similar conditions the endogenous alloxur bodies remain constant, but that they vary in different individuals.

As regards the exogenous urinary alloxuric bodies, these are derived from the alloxuric bodies present in the food. Different foodstuffs contain different quantities of these substances, and the whole of them are not excreted in the urine as alloxur bodies, some being broken up during the process of metabolism and excreted as urea. The authors carried out a series of observations on the effects of an ordinary meat diet consisting of ox flesh, calves' flesh, or ham, and the influence of such articles of diet as the thymus and the liver. The thymus is peculiarly rich in nuclein derivatives containing alloxur bases; and with thymus feeding the quantities of alloxur bodies in the urine undergo a very great increase, and about one-fourth of the quantity of alloxur bodies present in the thymus are excreted in the urine as such. Hypoxanthin is, however, the substance of most importance from this point of view, as it is present in considerable quantity in flesh, and it is the main cause of the increase in the uric acid excreted observed under a flesh diet; and it is also an abundant constituent of meat extracts. Hypoxanthin is excreted almost entirely as uric acid. The authors conclude that the exogenous urinary alloxuric bodies are derived from those already present in the food, and the quantities present in the urine are dependent solely on the nature of the ingested alloxuric body. They consider that about half of the alloxuric nitrogen of flesh, liver, spleen, etc., reappears as such in the urine; but that in the case of the thymus only about one-fourth, and that in all cases the increase is mainly in uric acid, the increase in the other alloxuric bodies of the urine being comparatively trivial.

The observations of these authors, then, would tend to the conclusion that diet plays a very great part in the metabolism of uric acid, but that it is possible to order a diet consisting of milk, bread, eggs, and certain vegetables, thanks to which, whatever excretion of uric acid occurs in the body must be entirely dependent on the formation of this substance from the tissues, and that such a diet may be looked upon as free from uric acid.

These observations place the treatment of certain cases of gout, gravel, and renal disease with a milk diet on a much more sound basis than has hitherto been the case. A milk diet cannot, however, be given indefinitely in adults, and its use must be restricted to acute cases, or, when given in chronic cases, to short periods. The uses of a vegetable diet in these diseases are also clearly brought out, and much benefit

may be derived from such a diet, not only by restricting the formation of alloxur bodies, but also owing to the alkaline salts present neutralizing the urine.

**Uric Acid and its Relation to the Biurates and to the So-called Quadriurates.** Although the formation of uric acid from the tissues of the body and from the ingested foods is of considerable importance, both in the pathology of gout and in that of gravel and calculus, yet it is possible that in all these diseases the actual conditions which lead to a deposition of the uric acid or its salts in the tissues or in the urinary channels are dependent rather on the factors which maintain the solubility of the uric acid than on the mere amount present. The pathology, therefore, of these diseases is associated not only with the question of the amount of uric acid present, but also with the question as to the form in which it exists in the blood and in the urine and the conditions which favor its deposition. Uric acid is universally recognized as a bibasic acid containing two replaceable atoms of hydrogen. If one of these is replaced by a base the acid urates are formed. On dissolving uric acid in free alkalies, a second atom of hydrogen is replaced by the alkaline metal forming what is known as a neutral urate. All observers, however, are agreed that these neutral urates are only formed in the laboratory and do not exist in the fluids and tissues of the body, either in physiological or in pathological conditions. Uric acid and its acid salts are relatively very insoluble; and, according to Bunge, a gramme of free uric acid requires, at the temperature of the room, about 14 litres of water to dissolve it, and at the temperature of the body 7 to 8 litres. A very large part of the problem of the pathology of gravel is dependent on this question of the solubility of uric acid and of its salts. The normal urine may contain as much as 2 grammes of uric acid dissolved in some 1500 to 2000 c.c. It is obvious from this that the uric acid cannot be dissolved as such, since even at the temperature of the body the 2 grammes of uric acid would require some 14 to 16 litres of water to dissolve it; whereas, as a matter of fact, it is dissolved in one-tenth of that quantity. This remarkable fact has been differently explained by different observers. According to some, the uric acid dissolved in the urine is in the form of a third order of salts, originally described by Bence Jones, to which the term quadriurate has been applied. This view has been accepted, apart from certain experimental evidence in its favor, on the ground that it is difficult to believe that the uric acid is dissolved in the urine in the form of the acid urate, owing to the fact that if the urine be allowed to stand without undergoing decomposition a large part of the uric acid is deposited in the form of free uric acid, and that the quantity so deposited from certain urines may amount to as much as 1 gramme. The alternative explanation to that which



regards the uric acid as existing in the form of a quadriurate is that the uric acid is in the form of acid urate of soda, and that this undergoes decomposition as a result of an interaction with the acid phosphate of soda present in the urine. A saturated solution of acid urate of soda, if mixed with a solution of acid phosphate of soda, will have an acid reaction, such as is the case with the urine normally. If this mixture be allowed to cool at the temperature of the room the reaction becomes alkaline, and free uric acid crystallizes out. This result is dependent on mass actions of uric and phosphoric acid. With the cooling of the fluid the mass action of the uric acid becomes less and that of the phosphoric acid the greater; the phosphoric acid then appropriates the alkali in the acid urate, forming the alkaline phosphate of soda and free uric acid. On warming the fluid some of the uric acid will dissolve, the mass action of the uric acid will increase, and the alkaline phosphate of soda will be decomposed in the inverse manner, with the formation of an acid phosphate and the re-solution of the uric acid in the form of acid urate. In the observations which are made on the mixture of solutions of acid urate of soda and of acid phosphate of soda the acid reaction of the fluid diminishes with the crystallization out of the free uric acid, owing to the formation of the alkaline phosphate. On the subsequent re-solution of the uric acid on warming the fluid becomes acid again. This interaction of the phosphates and the urates will, therefore, explain not only the solution of the large quantities of uric acid in the urine, but will also explain the deposition of uric acid when the fluid cools and its re-solution on warming.

At the present day, then, it may be said that these two views are current to explain the solution of these large quantities of uric acid in the urine. According to the one school, neither uric acid nor the acid urate of sodium exists normally in the fluids of the body, neither in the blood nor in the urine, the uric acid being in the form of a hypothetical quadriurate. According to the other, the uric acid is kept in solution in the tissues of the body, thanks to the presence and interaction of the phosphates and the urates. Such views as these must play a very large part not only in our notions as regards the pathology of gout and gravel, but still more with reference to our treatment of these conditions.

Although the quadriurate theory was in the first place evolved by Bence Jones, it has received its main support in late years from the work of Sir William Roberts. Bence Jones analyzed urinary deposits and, in confirmation of the observations of Scherer, found that the quantity of uric acid present was in excess of that required to form biurates with the bases present. He analyzed three specimens, and did not get concordant results in the three. In the first the proportion of uric acid to that required to form biurates was as 1 to 1.7; in the second, as 1

to 0.46; and in the third, as 1 to 1.04. The average of the three observations came out that the proportion was as 1 to 1.1. Bence Jones concluded from the analysis that a mixture of different amounts of urates and uric acid constitutes the amorphous sediment or urine; and, further, he concluded that this proportion nearly approximated to the proportions hypothetically required by a salt whose molecule consisted of one molecule of uric acid combined with one molecule of acid urate. Although the individual analyses, both of Bence Jones and of Scherer, varied considerably and gave very discordant proportions, the average of all the analyses yielded a proportion of uric acid which was nearly double the amount required to form biurates with the sum of the bases. It was this that led Bence Jones to the conjecture that a third order of uric-acid salts existed in which an atom of the biurate was loosely combined with an atom of free uric acid. Bence Jones, in order to test the soundness of his conclusions, attempted to form the quadriurates artificially. He succeeded in obtaining a substance which possessed some of the characters of the amorphous urate deposit in being granular in character and depositing free uric acid as a result of decomposition with distilled water. Bence Jones dissolved uric acid in potash and soda lye, and then he added either acetic acid or phosphoric acid until the liquid became slightly acid. In this way he obtained a dense precipitate, which he collected. He found that when he treated this substance with distilled water the amount that went into solution corresponded with the theoretical formula of potassium biurate, and that the uric acid which remained undissolved approximated in amount to that which went into solution as a biurate.

Although the results following the action of water on the amorphous quadriurate yielded results which were slightly discordant, the amount of uric acid that was thrown down and the amount remaining in combination as a biurate not being exactly equal, these discrepancies were explained on the hypothesis that the quadriurate was an exceedingly unstable salt, prone to undergo decomposition; and, therefore, that at different times it would contain varying quantities of free uric acid.

Sir William Roberts, in the Croonian Lectures of 1892, took up the question anew, and conducted a large series of observations tending to prove the existence of the quadriurates. He was unable to obtain constant results from the decomposition of natural amorphous urates, and in most cases the quantity of uric acid separated by the action of water was greater than that retained in solution; but this excess presented no uniformity. He was inclined to regard these discrepancies as dependent on the fact that the amorphous quadriurate was an unstable body, tending to constantly liberate free uric acid, and that, owing to the differences in the composition of the separate samples that had to be collected

from different patients at different times, in order to obtain a sufficient quantity for analysis, there would be great variation in its composition. Most of his observations were conducted on amorphous urates prepared artificially by using human urine, with the addition of bicarbonate of potash or soda to render it slightly alkaline, as a solvent of pure uric acid. It was not, however, necessary to add bicarbonate of potash or soda, as the alkaline urine passed after meals was also an efficient solvent for the purpose. The urine, either naturally or artificially alkaline, was raised to the boiling-point and shaken up with an excess of uric acid, and the mixture was allowed to cool and the precipitate collected. In this way not only were precipitates obtained closely analogous in character to the natural amorphous urates, but they yielded on analysis far more constant results as regards the proportion of uric acids; and he considers that his results confirmed the view of Bence Jones that a third order of salts existed to which the name of quadriurate was applicable. Sir William Roberts showed that these quadriurates underwent a series of decompositions under different circumstances, leading in the one case to the liberation of free uric acid, as, for instance, by the action of distilled water; and, on the other hand, if acted upon by alkaline menstrua, such as the blood serum, they would yield crystals of the biurate of soda. His experiments undoubtedly threw a very great light both on the pathology of gout and on that of gravel, showing how the mere reaction of the medium tended in the one case to produce a deposit of acid urate of soda, and on the other hand, free uric acid. He explained in a masterly way how, given an excess of quadriurates in the blood plasma, there would of necessity result in time a precipitation of acid urate of soda, and how an excess of quadriurates in the urine or a deficiency of saline ingredients in the urine would tend, on the other hand, to the liberation of free uric acid.

Although these observations did not explain in any way the mode in which an excess of uric acid was produced in the blood, they yet explained in a very complete manner how such an excess would produce, on the one hand, a fit of gout, or, on the other hand, an attack of gravel. A large number of observers of recent years have accepted the hypothesis of the existence of these quadriurates, although some observers have criticised them. One criticism especially has been raised, namely, that inasmuch as the quadriurates, from the mode of their formation, required the existence of a slightly acid medium, it was difficult to see how these substances could exist as such in the blood.

Tunncliffe and Rosenheim<sup>1</sup> have recently investigated the question anew. They have prepared the amorphous urates by the methods de-

<sup>1</sup> *Lancet*, June, 1900.

scribed by Sir William Roberts and have analyzed them again, and they conclude that neither by the acetate nor the phosphate method could they prepare precipitates which corresponded in composition to the hypothetical quadriurates. One of their most important conclusions is that in all the cases in which the hypothetical quadriurate was formed by the phosphate method a certain amount of phosphoric acid was always present in the salt obtained. In the case of the sodium salts with the phosphate method they concluded that the substance was not a quadriurate, but that it consisted of a mixture of phosphate of sodium, free uric acid, and biurate of sodium; and in the case of the potassium salt that the substance was a mixture of uric acid and biurate. They conclude, finally, that the substances obtained artificially under the conditions supposed to produce quadriurates consist of mixtures in varying proportions of uric acid and biurates or of pure uric acid or pure biurates.

An analysis of a natural urinary sediment yielded results showing that phosphoric acid was present, and that the sediment consisted to a great extent of free uric acid mixed with the biurates of sodium, potassium, ammonium, and magnesium, with some phosphate of calcium; and that the proportion of combined to free uric acid was as about 1 to 4.

The decomposition of the hypothetical quadriurates by the action of water into free uric acid and biurate of sodium has hitherto been looked upon as a more or less characteristic reaction. Tunncliffe and Rosenheim, however, look upon the formation of uric-acid crystals from these precipitates by the action of water as dependent on the fact that the uric acid is present in an amorphous form; and in support of this they adduce the fact that the quantity of uric acid formed in different samples varies. They regard the fact that it is sometimes present in approximately equal amount to that remaining in the form of a biurate as only accidental. They have also prepared a so-called quadriurate yielding by the action of distilled water free uric acid and biurate under circumstances where, *ex hypothesi*, a quadriurate could not be formed. This was done by taking a saturated solution of a biurate at the boiling-point and treating it with an excess of uric acid also at the boiling-point. Under these circumstances a quadriurate could not be formed, inasmuch as it would be decomposed by boiling water. Nevertheless, on cooling a solution made as above described, an amorphous precipitate was formed, which under the microscope showed the characteristic decomposition on the addition of water, yielding crystals of uric acid. This certainly is strong evidence in favor of the view that the formation of crystals by the action of distilled water on the amorphous deposit is really dependent on the presence of uric acid in an amorphous form,

and that it cannot be taken as evidence that the amorphous deposit was really a quadriurate.

From Tunnicliffe's and Rosenheim's observations it must be concluded that the evidence of the existence of a third order of salts of uric acid is very considerably shaken, and that we must perhaps revert to the older view of Bunge and others, that the uric acid exists in the body in the form of a biurate of soda, which is kept in solution and undergoes decomposition in such fluids as the urine by an interaction between the urates and the phosphates.

**Diuretics.** Diuretics are used not only for the purpose of relieving renal dropsy, both in acute and in chronic disease, but also for a variety of other purposes, as, for instance, to dilute the urine, to relieve partial or complete suppression, and they have been used occasionally in the treatment of serous effusions. They are certainly of no avail in the treatment of inflammatory effusions, and it is more than doubtful whether diuretics have any marked effect in procuring the absorption of such chronic effusions as ascites or hydrothorax. Hence, the main objects of diuretics are to relieve suppression, to dilute the urine, and to relieve dropsy. Axtell<sup>1</sup> considers the action of these substances more especially from the point of view of their use in the relief of renal dropsy, where their action, however, is very uncertain, probably owing to the different conditions obtaining in dropsy accompanying acute and chronic renal disease. Dropsy in acute nephritis is always, and in chronic nephritis is sometimes, a true renal dropsy; but in some forms of chronic renal disease the dropsy is of cardiac origin. Hence, just as in heart disease we may meet with cases of cardiac or of renal dropsy, so in renal disease the dropsy may really be of renal or of cardiac origin. Both in cardiac and in kidney disease dropsy of true renal origin is more refractory to treatment than that which is dependent on cardiac causes. Inasmuch as the dropsy of renal disease is at any rate not dependent primarily on the mere diminution in the amount of urine secreted, and inasmuch as complete suppression is not usually accompanied by any material amount of dropsy, it is at once clear that substances acting on the kidney and promoting an increased excretion of water can really only indirectly influence the amount of the dropsy. Pathologists are agreed that true renal dropsy must be dependent on some change in the relationships existing between the blood and the bloodvessels, so that the fluid inside the bloodvessels is allowed to transude into the lymph-spaces of the tissues in increased amount. Hence, in renal dropsy the diminution in the flow of urine, although varying directly with the amount of the dropsy, may be looked upon rather as a result

<sup>1</sup> Medical News, January, 1900.

than as a cause of the dropsy; in other words, the dropsy of renal disease is in all probability a toxic dropsy, and although the toxic agent may be retained in the circulation and produce its effects, owing to the want of its excretion by the kidney, yet the diminished quantity of urine secreted by the kidney is really rather a result of the dropsy than its cause. This view of the pathology of renal dropsy is one that does not make the use of diuretics for the relief of renal dropsy a very hopeful one. Another objection to the use of diuretics to relieve renal dropsy is that the kidney is in a more or less damaged condition; and one of the fundamental principles of the treatment of diseases is to rest, or not to excite, an organ that is in a state of inflammation. This objection in the case of the kidney is, perhaps, to a large extent a theoretical one; but still many substances which act as diuretics in certain doses, in other doses may produce inflammation or even suppression of the renal functions.

There is at present no satisfactory classification of diuretics. Axtell divides them into saline diuretics and stimulant or irritant diuretics, although the latter group, at any rate, includes a number of substances which have very different actions pharmacologically. The saline diuretics are those which are generally used for the relief of the dropsy of acute nephritis when this mode of treatment is adopted. It is thought by many that saline diuretics are not of so much avail in the relief of the dropsy of chronic renal disease. Caffeine and digitalis are substances having, in certain circumstances, very powerful diuretic properties. Caffeine is, perhaps, the substance with the most powerful diuretic action, but its use is often very limited, owing to the fact that the action that it produces on the kidney is really a double one, and it is only in certain doses that its full diuretic action is obtained. Caffeine is a body which certainly deserves the title of a stimulant diuretic, owing to the fact that it not only produces its effects by acting on the circulation, but it also increases the activity of the special excretory cells in the convoluted tubules. Caffeine in small doses causes a very notable expansion of the kidney, which can be determined experimentally. In large doses, or, what is still more important, in repeated small doses, it no longer causes expansion of the kidneys, but contraction, with diminution or even suppression of the urinary excretion. Small and initial doses of caffeine often produce marked results clinically in relieving dropsy both of renal and of cardiac origin; but it is a common experience to find that the drug soon loses its beneficial action, and that frequent and repeated doses are often followed by slight toxic effects. The results of clinical experience and those of the laboratory really coincide, and caffeine is a substance which should be used discontinuously, and certainly it is not a drug which should be adminis-

tered to relieve the dropsy of acute renal disease; not only because it is a stimulant of the kidney, but also because it is a substance containing alloxur bases, and at any rate a portion of it is excreted in the form of urea. Hence, it not only stimulates the kidney, but at the same time it increases the amount of work which the kidney has to do. Digitalis, on the other hand, is a substance which has no right to the title of diuretic, inasmuch as it not only does not increase the excretion of urine in health, but its action in increasing the excretion of urine in disease is entirely dependent on the effects which it produces on the circulation by raising the blood-pressure, partly by contracting the peripheral vessels, partly by increasing the force of the heart-beat, so that the circulation, after the administration of digitalis, is a far more vigorous and efficient one. As a result of this, digitalis is not only of use in the relief of cardiac dropsy, but it may also, in certain selected cases, be of use in the relief of renal dropsy, more especially where that dropsy supervenes in chronic renal disease as a result of cardiac failure. Its administration here, however, is fraught with difficulties, owing to the fact that in renal disease the blood-pressure may be already high, and the heart may be failing as a result of degenerative changes dependent on this pressure, and digitalis is a substance which, although it will stimulate the heart, will at the same time increase the amount of work that the heart has to do. Notwithstanding this objection, digitalis may be of service for the relief of dropsy in renal disease where the heart and circulation show signs of failure. Diuretics, in the true sense of the word, are, therefore, of little avail in the treatment of the dropsy of acute renal disease. They are, however, of more use in the treatment of the dropsy of chronic renal disease, both when it is of renal origin and when it is of cardiac origin. The dropsy of acute disease should be treated rather by measures tending to promote the excretion of the retained fluid by other channels, and more especially by the skin and the bowel.





# PHYSIOLOGY.

By ALBERT P. BRUBAKER, M.D.

## GENERAL PHYSIOLOGY.

**On the Nature of the Process of Fertilization and the Artificial Production of Normal Larvæ (Plutei) from the Unfertilized Eggs of the Sea-urchin.** Some of the most interesting work of our age—in fact, experiments worthy of the closing years of the nineteenth century—is that of Prof. Loeb<sup>1</sup> on the artificial production of normal larvæ from the unfertilized eggs of the sea-urchin. It has been said that bacteriology and pathology, the two sisters that the nineteenth century was so proud to beget, have had their day, and that the era of physiological chemistry has come. Loeb's record-breaking work seems to more than justify the statement, because he has produced what would be ridiculed if it had not been accomplished, namely, chemical fertilization without the aid of spermatozoa. His experiments began eight years ago with the recognition of the effects that an increase of concentration of sea-water would have upon the segmentation of the fertilized eggs of the sea-urchin. From this he was led to try the effects of sea-water with varying proportions of its salts and with salts not normally in the sea-water. Morgan,<sup>2</sup> who confirmed many of Loeb's previous experiments, now tried the effect of an increase of different salts on the *unfertilized* eggs of the sea-urchin. He found that eggs that were put into sea-water whose concentration had been raised by the addition of 1.5 per cent. of NaCl or 3.5 per cent. of MgCl<sub>2</sub> began to segment into two or more cells when put back into normal sea-water. This segmentation went on in some cases about as far as the 64-cell stage, but then the development stopped. Loeb took up this line of experimentation and brought the *unfertilized* eggs to a healthy larval stage.

In order to avoid innumerable possible sources of error—that is, possible sources of spermatozoa contamination—the experiments were done on a very large number of eggs over many series, and have already been confirmed by Morgan working independently. To review this series of experiments would require more space than is at our disposal,

<sup>1</sup> American Journal of Physiology, 1899, vol. iii., pp. 135, 434.

<sup>2</sup> Archiv f. Entwicklungsmechanik, 1899, vol. viii., p. 448.

and the reader is referred to the very interesting and complete original papers. An abstract of his conclusions is : From these experiments I draw the conclusion that by putting the *unfertilized* eggs of the sea-urchin for two hours into a solution of 60 c.c.  $\frac{2}{8}$  normal  $MgCl_2$  + 40 c.c. of sea-water the eggs develop into blastulæ if brought back into normal sea-water. If we put the unfertilized eggs for about two hours into a solution of equal parts of  $\frac{2}{8}$  normal  $MgCl_2$  and sea-water the eggs may reach the pluteus stage. The plutei produced from the unfertilized egg resemble closely in every respect those produced from the fertilized egg. The latter in many cases live longer than the former, but even this was not so in every case, and it is not impossible that in further experiments pathogenetic plutei with a greater duration of life will be produced.

These facts force us to transfer the problem of fertilization from the realm of morphology into that of physical chemistry. There is certainly no reason left for defining the process of fertilization as a morphological process. The morphology of the spermatozoön itself becomes of secondary importance as far as the process of fertilization is concerned. The spermatozoön not only starts the development of non-pathogenetic eggs, but it is also the bearer of the hereditary qualities of the male. From these experiments it becomes evident that these two functions of the spermatozoön are not necessarily bound together, for nobody would assume for an instant that the hereditary qualities that are carried by the spermatozoön could be imparted to the egg by a change in the inorganic constituents of the sea-water. We have learned to attribute the different activities of cells to different enzymes ; we must in future consider the possible or probable separation of the fertilizing-qualities of the spermatozoön from the transmission of hereditary qualities through the same.

**Ion-proteid Compounds and their Role in the Mechanics of Life Phenomena.** One of the factors that aided Loeb's<sup>1</sup> work was his discovery of the rôle of the ion-proteid compounds in the mechanics of life phenomena. It was found that the salts or electrolytes in general do not exist in living tissues as such exclusively, but are partly in combination with proteids. The salt or electrolytic molecules do not enter into this combination as a whole, but through their ions. The great importance of these ion-proteid compounds lies in the fact that by the substitution of one ion for another the physical properties of the proteid compounds change ; for instance, their power to absorb water and their state of matter.

Thus these ion-proteid compounds present to us essential constituents of living matter which can be modified at desire, and hence enable us

<sup>1</sup> American Journal of Physiology, 1900, vol. iii., p. 327.

to vary and control the life phenomena themselves. This study of the ion-proteids showed that a pure solution of NaCl was of the same concentration as sea-water for many, if not all, marine animals. The poisonous effects of this solution are due to the Na-ions. The same is true for pure equimolecular solutions of CaCl<sub>2</sub> and KCl. The poisonous effects of the Na-ions are antagonized by the addition of a small amount of Ca-ions and K-ions. Through the presence of these two ions the Na-ions in the ocean lose their poisonous effects. The Na-ions of the blood would not allow the tissues to live; but the presence of Ca-ions, K-ions, and possibly other ions counteract the poisonous effects of Na-ions in the blood. This is the reason why tissues live longer in Ringer's solution than in a physiological salt solution.

**On the Different Effects of Ions upon Myogenic and Neurogenic Rhythmical Contractions and upon Embryonic and Muscular Tissue.**

In still another paper bearing the preceding title Loeb<sup>1</sup> traces up the conclusions arrived at in the preceding papers. He says: The facts already demonstrated support the assumption that irritability depends upon the various ions, especially the metal ions (Na, Ca, K, and Mg), existing in definite proportions in the tissues; but as each tissue has its own specific irritability, it would follow that the various tissues must possess the various ions in different proportions. In other words, it is not the histological or morphological structure of the ganglia in the case of nervous impulses which allows them to be so important, but their chemical constitution. This does not mean that Ca-ions or any other ions are the cause of or the stimulus for the rhythmical contractions (in the case of the heart, for instance); but it assumes that for the possibility of rhythmical contractions the Na-ions, Ca-ions, and K-ions must exist in certain definite proportions. The phenomena of muscular contractility and the phenomena of cell division are considered by many authors as being of the same order. The rays of the astrophere are said to be contractile fibrils which pull the chromotomes apart and accomplish the division of the mother cell into two daughter cells. Loeb denies that this hypothesis can be harmonized with the fact that enormous quantities of K-ions in no way interfere with the process of karyokinesis, while even much smaller amounts of K-ions annihilate muscular activity in a very short time. Still, this new study of the ions is too comprehensive to be studied from abstracts, and the reader will find his time well spent in a perusal of the original articles.

**Facts and Laws of Heredity.** The theory of Weismann that heredity is simply a function of the sexual cells; that the whole organism and its constitution play no part in the phenomena of heredi-

<sup>1</sup> American Journal of Physiology, vol. iii., p. 383.

tary transmission, and that, therefore, the individual development of the parental organism and the changes acquired during development produce no influence on the organism of the descendants, is too dogmatic, according to the facts observed by Orchansky.<sup>1</sup> This observer reduces the theory of heredity to the following theses: 1. Heredity is a direct function of the sexual cells and an indirect function of the whole organism, the former being the foundation for the stability of the type, the latter accounting for the individuality or variability. 2. The direct heredity is more powerful than the indirect. 3. The character of heredity is different for the two kinds of sexual cells, and corresponds to the nature of their structure. 4. The energy with which the indirect heredity strives to transmit itself is the greater; the smaller the individual changes the more general their character and the earlier their appearance. 5. Modifications coming on during the maturer years of the organism, and especially accidental pathological changes, cannot be transmitted to the descendants.

### METABOLISM.

**The Influence which the Amount and Kind of Food Exert upon the Degree of Metabolism and Functional Activity.** In reply to the criticisms emanating from the laboratory of Carl v. Voit, Pflüger<sup>2</sup> has reinvestigated this subject, and has come to the following conclusions:

1. An addition of albumin to a maintaining diet causes a higher metabolism and functional activity of the animal.

2. An addition of albumin to a maintaining diet causes an increase in the body-weight, on account of an increase of cellular substance, and this increase may, under favorable conditions, go on until the body-weight is doubled or more.

3. The metabolism and the functional activity of the animal increase proportionally to the increase of body-weight produced by albumin. Both of these physiological conditions, therefore, can be produced only by a more plentiful supply of albumin in the food.

4. Every decrease of the daily introduction of albumin causes a decrease of the metabolism and the functional activity, even if fat and carbohydrates having the same amount of energy as the albumin withdrawn are given.

5. The additional introduction of fat and carbohydrates is not followed by an increase in metabolism nor by an increase in the material value of the organs.

<sup>1</sup> Arch. f. Physiologie, 1899, Heft 3 and 4, S. 214.

<sup>2</sup> Pflüger's Arch. f. d. ges. Physiologie, Band lxxvii., S. 521.

6. Each additional amount of albumin pushes from the metabolism an amount of fat which possesses the same content of energy.

7. The laws of proteid metabolism are the same in the dog as in the cat.

8. There is no development of fat from albumin in the animal body, as Voit asserts.

9. Man cannot satisfy his entire need for food with albumin alone, because he cannot digest the amount which would be required.

According to Pflüger's investigations, young men, living only according to their instincts, cover about one-fifth of their need with albumin. As, however, man can digest much more albumin, it seems that the profitable value which is caused by the increased albumin has an upper limit in omnivorous animals, because instinct objects to an exclusive meat diet.

**Experiments on Metabolism with Proteids Containing Phosphorus and Those Free from It.** These experiments were made by Zadik<sup>1</sup> on dogs. These were fed for a certain time on a diet just sufficient to maintain the metabolism. The food contained alternately but a single proteid casein containing phosphorus and edestin, the crystalline proteid of hemp-seed, entirely free from phosphorus. When feeding the edestin there was added to the food, however, an amount of phosphorus in the form of a phosphate equivalent to that contained in an organic form in the casein. From many experiments the author concludes that the animal organism does not possess the power to form synthetically from proteids, free from phosphorus and phosphates, the phosphor-holding organic combinations necessary to the life of the cell.

**The Sexual Function and Metabolism.** The assertion of Brown-Séquard, the discoverer of internal secretion, that "*Les sécrétions internes soit par une influence favorable direct soit en empêchant des actions nuisibles, semblant être d'une grand utilité pour maintenir l'état normal de l'organisme,*" has been verified, especially with reference to the thyroid gland. Loewy and Richter<sup>2</sup> have endeavored to establish a corresponding relation between the ovaries and the general metabolism of the body. From their experiments made on dogs they deduced the following conclusions:

1. After castration there is found after a long time a distinct reduction in the exchanges of gases.

2. The administration of oöphorin, if begun even two and a half or three months after the operation, not only prevents this reduction, but even produces a distinct increase in the metabolism far beyond that observed

<sup>1</sup> Pflüger's Arch. f. d. ges. Physiologie, Band lxxvii., S. 1.

<sup>2</sup> Arch. f. Physiologie, Supplement, 1899, Band i., S. 174.

before the operation. This increase may continue for a time after the withdrawal of the oöphorin, though it will gradually decline.

3. In the normal animal oöphorin does not exert any influence on the exchange of the respiratory gases.

4. The same negative result is observed after giving the organic preparations from the male sexual glands to castrated female animals.

**The Reaction of the Animal Organism toward Foreign Blood-serum.** From a series of experiments, made with a view of testing the toxicity of blood-serum, by Friedenthal and Lewandowsky,<sup>1</sup> the following conclusions may be drawn :

1. The sera of animals of the opposite sex do not show any specific differences, and they may be substituted one for the other, contrary to the statements of Weiss.

2. The serum of one animal is toxic in the circulation of another animal of a different species ; the degree of toxicity, however, is variable.

3. By heating the serum to 58° or 60° C. for some time its toxicity is completely removed.

4. Serum freed from its toxic agent is taken up by the organism, and even in large amounts, without any subsequent reaction. Its proteid matters are completely oxidized.

Clinically interesting is the fact that a natural foreign serum was found to be much less toxic when given subcutaneously. Thus, a rabbit of 900 grammes weight could stand as much as 20 c.c. of active calf-serum injected beneath the skin of the back without showing any signs of albuminuria. As horse-serum is less toxic than calf-serum, it is easy to understand how little danger there could be from the injection of a few cubic centimetres of antidiphtheritic serum, as far as the fact of foreign serum is concerned.

**The Origin of Uric Acid from Nuclein Compounds and their Derivatives.** The modern theory of the origin of uric acid from nucleins has been so well established that during the past year but little new work in support of it has been done. Still, the position does not remain unchallenged, and Jerome<sup>2</sup> has taken up the gauntlet against some of the objections to the theory. It was affirmed by Hopkins and Hope that for substantial support the theory depended almost entirely on experiments with calf's thymus ; thereupon Jerome shows an increase of uric acid after the ingestion of pig's pancreas, herring's roe, and Liebig's extract of meat, in all of which the presence of a nucleoproteid was proved in advance.

Two other objections, namely, that the disproportion between the

<sup>1</sup> Arch. f. Physiologie, 1899, Heft 5 and 6, S. 531.

<sup>2</sup> Journal of Physiology, vol xxv., p. 98.

small amount of nucleoproteid in muscle and the relatively large increase of uric acid which follows a meat diet is not to be explained by the nuclein theory of the origin of uric acid; and that as nuclein resists digestion with pepsin-HCl, it cannot be expected to supply the uric which is excreted a few hours after a meal, he answers by saying that the presence of alloxin bases, especially hypoxanthin, in flesh diet probably accounts for the early rise in uric-acid excretion after a meal. He concludes, affirming that while there is convincing evidence that uric acid may be formed from nucleoproteid nuclein and one variety, at least, of alloxur base, there is at present no proof that it can arise in man independently of a substance containing an alloxur or purin group.

**The Uric-acid Deposits Artificially Produced in Birds.** Schreiber and Landy<sup>1</sup> confirm by their experiments the investigations and theory of Ebstein, according to whom uric acid plays an important part in the causation of gout. The tissue juices saturated with uric acid produce necrosis, in which necrotic areas the uric acid formerly held in solution is now deposited. These authors thus disprove the criticisms which Likhatscheff, Riehl, and His had made against the views of Ebstein.

**The Significance of Cola, Coffee, Tea, Mate, and Alcohol for the Function of the Muscles.** By means of work performed with Mosso's ergograph, Schumburg<sup>2</sup> found that pure infusions of coffee, tea, and maté, and probably also of cola, do not have a stimulating effect on the completely exhausted body unless at the same time nutriments—carbohydrates, fats, and proteids—are also supplied. Alcohol does not seem to be a nutriment like the carbohydrates, which liberate energy by their oxidation. Alcohol, perhaps, is rather to be regarded like the excitants just mentioned; it shows its effect if at the same time the usual nutriments are taken.

**The Amount of Fat in the Glands During the State of Hunger.** Nikolaides<sup>3</sup> has observed that during hunger there is always an accumulation of fat in the cells of the glands of the mouth, stomach, intestine, pancreas, liver, etc. The fat granules are arranged in two series—one close to the basement membrane, the other close to the lumen. While there is plenty of fat, however, in the glands just mentioned, which during hunger have little or no functional activity, there is no fat in those organs which have to do a large amount of work. Thus the muscles of the hungering animal do not show the presence of any fat granules, which, however, at the same time abound in the gland cells. The author believes from his experiments that the fat found in the glands does not wander there from the subcutaneous tissue, but is

<sup>1</sup> Pfüger's Arch. f. d. ges. Physiologie, Band lxxix.

<sup>2</sup> Arch. f. Physiologie, Supplement, Band ii.      <sup>3</sup> Arch. f. Physiologie, 1899, S. 518.

produced in the cells themselves by a transformation of the albumin of the protoplasm into fat. He further believes that this fat wanders from the glands as well as from the subcutaneous tissue into the organs, where life-processes under the circumstances mainly take place.

**The Supposed Albumin-saving Action of Alcohol.** The question as to what influence alcohol has on the human metabolism must be subdivided into the following three questions: 1. Is alcohol consumed in the body at all? 2. What effect has alcohol on the intake of oxygen and the output of carbon dioxide? 3. How does alcohol influence the albumin metabolism? Rosemann<sup>1</sup> considers the first two questions as definitely settled—alcohol is consumed in the body, and it changes neither the intake of oxygen nor the output of carbon dioxide. With regard to the third question, he agrees with Miura, Schmidt, and Schoeneseifer, who have also shown that alcohol is incapable of preventing albumin metabolism.

**The Influence of Alcohol on the Secretion of Milk.** Rosemann<sup>2</sup> had at his disposal a number of cows which were kept under extremely favorable conditions. He concludes from many experiments on these animals that alcohol has no favorable influence on milk secretion. He further believes that these results may be applied to the nursing woman. To those who are not accustomed to the use of alcohol it is unnecessary to take alcohol for this purpose; but, on the other hand, it need not be forbidden to those who take wine or beer habitually, because with moderate doses no alcohol enters the milk; only with excessive amounts may as much as 0.2 to 0.6 per cent. be excreted by the mammary gland.

### DIGESTION. ABSORPTION.

**The Influence of Bile, of Acids, and of Alkalies on the Proteolytic Action of Pancreatic Juice.** From a series of experiments made last year Chittenden and Albro concluded that the addition of fresh bile to a neutral pancreatic extract does not give rise to any great degree of stimulation—*i. e.*, the proteolytic digesting power of the enzyme is not markedly increased, and they further added that in no one of their experiments did they find a confirmation of the results reported by Rachford and Southgate (in 1895), who found on an average that the proteolytic action of pancreatic juice was increased one-fourth by the addition of bile. With the publication of these experiments Rachford<sup>3</sup> repeated his investigations and reiterated his conclusions of 1895.

<sup>1</sup> Pflüger's Arch. f. d. ges. Physiologie, Band lxxvii., S. 405.

<sup>2</sup> Ibid., lxxviii., S. 466.

<sup>3</sup> Journal of Physiology, 1899, vol. xxv., p. 165.



Moreover, all of Rachford's experiments were done with fresh pancreatic juice and fresh bile, consequently he affirms that his conditions resembled more nearly nature's than those of Chittenden and Albro, who used pancreatic extract. Moreover, the latter authors, inferring that the contents of the duodenum are generally alkaline, found that a few thousand of 1 per cent. of combined hydrochloric acid sufficed to exert an inhibitory influence on pancreatic proteolysis, and with a sufficient amount of combined acid alone proteolysis may be almost completely checked. Rachford takes this up first by denying that there is any evidence to prove that the duodenal contents in the carnivora are generally alkaline; and by experiments he proves that when rabbit's pancreatic juice is added to fibrin, one-half saturated with combined hydrochloric acid, it will do almost as much work in proteolysis as when added to neutral fibrin, and only after the fibrin is nine-tenths saturated with hydrochloric acid is the proteolytic action of the juice retarded; that combined hydrochloric acid when not greater than one-half saturation, provided bile be added, causes an increase in proteolysis.

Others of Rachford's experiments go to show that not only will combined hydrochloric acid not destroy the proteolytic action of pancreatic juice, but that even free hydrochloric acid, though it will greatly inhibit, will not destroy its action.

Rachford's experiments included also the influence of bile on proteolysis carried on by organized ferments. They demonstrated that bile retards such fermentation. In the course of the work it was seen that the proteolytic action of pancreatic juice is greatly weakened by dilution, and "on theoretical grounds this would seem to be a serious drawback to thorough proteolysis in the intestinal canal, since this process requires hours for its completion, and occurs not alone in the duodenum, but probably throughout the greater portion of the small intestine. These references and deductions naturally suggested an inquiry into the influence which the sodium carbonate and alkaline intestinal contents for the lower ileum and jejunum might have upon the proteolytic action of pancreatic juice." Experiment showed that sodium carbonate exercised a very favorable influence on the proteolytic action of dilute solutions of pancreatic juice.

**The Chemical Reaction of the Intestinal Contents.** In connection with the chemical reaction of the normal duodenal contents it is interesting to note the work done in relation to it by Moore and Bergin.<sup>1</sup> They tested the duodenal contents in sheep, calves, and dogs at different locations under various conditions of diet with methyl-orange, lacmoid, litmus, and phenolphthalein. From 8 to 10 cm. below the pylorus the

<sup>1</sup> American Journal of Physiology, 1900, vol. iii., p. 316.

reaction was alkaline in all cases to the first three and acid in all cases to phenolphthalein. From experimentation with the four indicators employed on different alkaline and acid solutions it was thought that the acidity represented by the phenolphthalein was due to dissolved carbonic acid. They conclude, therefore, that the invariable alkaline reaction to methyl-orange, lacmoid, and litmus shows the absence of hydrochloric acid and of all stronger organic acids, such as acetic, lactic, or butyric, which would be formed in bacterial decomposition of carbohydrates or fats.

**Auto-intoxication as the Cause of Pancreatic Diabetes.** Tuckett,<sup>1</sup> in a short preliminary communication, makes pancreatic diabetes the result of auto-intoxication. He found that lymph from the thoracic duct of a dog in full digestion, if injected into the portal circulation, will cause glycosuria, but that thoracic lymph from a fasting dog will not; in fact, if the latter thoracic lymph is injected into a dog suffering from pancreatic diabetes it will cause a lessening of the glycosuria. From these experiments he argues that the pancreas has an internal secretion ( $\pi$ ), which enters the circulation constantly by way of the thoracic lymph, and that a toxic substance ( $\tau$ ) capable of causing glycosuria, if not neutralized by  $\pi$ , is absorbed from the intestine during digestion by way of the lymph stream. The former is constantly being secreted in small quantities from the pancreas, and gradually accumulates in the blood; the latter is a periodic (digestive) product from the intestine, and entering the thoracic duct in such large amounts that it remains unneutralized until it reaches the blood. Pancreatic diabetes is established by a disturbance of the normal balance between  $\pi$  and  $\tau$ .

**Intestinal Absorption and Saline Cathartics.** Wallace and Cushing<sup>2</sup> severely criticise the view of Höber, according to which the absorption of saline solutions in the small intestine can be reduced to purely physical factors, the absorption being directly proportional to the velocity of diffusion. They refer to their former experimental work, described in the *American Journal of Physiology*, vol. i., p. 44, and here bring new experimental proof for their own theory. According to them, it is improbable that the intestinal epithelium is entirely passive in the selection of the offered solutions, because other cells, as the erythrocytes, take up certain salts and reject others. They conclude that the intestinal absorption cannot be explained by purely physical forces, as the difference in physical relations between such salts as sodium butyrate or coprate and the sodium chloride is certainly much greater than that between the sodium chloride and the sodium fluoride or the sodium sulphate, and

<sup>1</sup> *Journal of Physiology*, vol. xxv., p. 63.

<sup>2</sup> *Pflüger's Arch. f. d. ges. Phys.*, Band lxxvii., S. 202.

yet the solutions of the first three salts are absorbed equally rapidly, those of the two latter much more slowly or hardly at all. That the physical forces do not suffice to explain absorption is not meant to convey the idea that the intestinal cells take up solutions by means of vital forces. The experiments made recently in reference to the absorption of salts by living tissues appear to indicate that the colloidal substances stand in certain chemical relations to the cells, as they take up one salt easily and refuse another.

This selection can be explained not by the physical, but only by the chemical properties of the salts, and seems to be different in different cells. The experiments performed with the newer physical methods regarding the relation of the salts to the living tissues cannot explain the movement of fluids in the body, but only put in a clearer light the co-operation of the chemical affinities of the proteids.

### BLOOD. CIRCULATION. RESPIRATION.

**The Origin of Fibrinogen.** In an elaborate series of experiments after a complete study of similar work in the literature Mathews<sup>1</sup> demonstrates, so that it can scarcely be doubted, the origin of fibrinogen, and his conclusions give him the opportunity to theorize on the functions of the leucocytes. His general observations in the course of the experiments are as follows: The lack of fibrinogen when removed from the blood of cats by repeated bleedings, defibrinations, and re-injections, appears to cause no serious or characteristic symptoms. After defibrination the fibrinogen is rapidly re-formed, and in two or three days is present in normal or more than normal amounts. This re-formation takes place normally in the absence of the spleen, the pancreas, the kidneys, the reproductive organs, or the brain. Hence, these organs cannot be important makers of fibrinogen. There is no re-formation, or this re-formation is at a greatly reduced rate, if the small and large intestine be removed.

The paraglobulin of the blood is not converted into fibrinogen outside the body or by the vascular endothelium, the skeletal muscles, skin, or other tissues of the leg; nor is fibrinogen formed in this region of the body, because in prolonged perfusions of the leg with defibrinated blood no fibrinogen is added to the blood. The blood of the inferior vena cava, both below and above the kidney, is poorer in fibrinogen than the carotid blood. The blood of the mesenteric vein is constantly somewhat richer in fibrinogen than the arterial blood. Fibrinogen is not derived directly from the proteid constituents of the food, since it is readily re-formed after six to ten days' fasting, nor does the fibrinogen content

<sup>1</sup> American Journal of Physiology, 1899, vol. iii., p. 53.

of the blood diminish during fasting. There is no direct relationship between the number of leucocytes in the blood at a given time and the percentage of fibrinogen. A small number of leucocytes may coincide with a heavy fibrinogen percentage, and *vice versa*. Yet if leucocytosis be prolonged for several days by suppurations induced by setons, plasters, local infections, etc., the fibrinogen content of the blood increases, and in this respect running a parallel course with uric-acid excretion. If the intestinal area be excluded from the circulation the clotting of blood is greatly retarded. Finally, the general features of blood clotting bear a striking resemblance to those of indirect cellular division or karyokinesis, for reasons which the author is able to parallel very clearly, the principal one being that there is present in the cell body of the leucocyte a substance which by the action of a substance coming from the nucleus or arising in its neighborhood is thrown into a fibrillar form closely resembling fibrin fibrils, and, like them, contractile.

From these observations Mathews concludes that the decomposing leucocytes of the blood, and chiefly those of the intestinal area, are clearly the source of the fibrinogen of the blood; though taking this conclusion as a fact, the author is unable, however, to definitely state the manner in which the fibrinogen is constantly being disposed of or whether it is to be regarded as a food or not. If paraglobulin be also derived from the leucocytes, as Schmidt's and Mörner's observations indicate, then it would appear as if the proteids of the blood are derived directly from the leucocytes, Hoffmeister's view, that the absorption and assimilation of proteids is a function of the leucocytes, would thus be considerably strengthened. The suggestion is also offered that the leucocyte is the storehouse of the surplus proteid food of the body, just as the liver cell is the storehouse of surplus carbohydrate food.

**Secondary Rhythms of the Normal Human Heart.** Lombard and Pillsbury<sup>1</sup> have added, in an interesting paper, something to the physiology of secondary rhythms of the normal human heart. They claim that the rate of beat of the normal human heart when the subject is at rest undergoes two forms of periodic variation. One of these changes of rate is associated with the action of the respiratory centre, and may be called the respiratory rhythm; the other corresponds to changes in the volume of the finger attributable to vasomotor activities, and may be termed the vasomotor rhythm. These statements are based on experiments made on five men from twenty-one to fifty years of age. They conclude that these secondary rhythms of the heart are due to the overflow of impulses which originate in the respiratory and vasomotor centres, and which act upon the vagus centres.

<sup>1</sup> American Journal of Physiology, vol. iii., p. 201.

Inspiratory activity of one of these centres and vasoconstrictor activity of the other act alike to inhibit the inhibitory centre of the heart, and thereby quicken the heart-rate. The time of action of these two sets of influences as well as their intensity is of importance, for they may aid or oppose each other and produce correspondingly large or small effects.

Though corresponding in general time, the vasomotor changes of the volume of the finger of the Traube-Hering type and the vasomotor rhythm of the heart do not stand primarily in causal relation to each other, but each is the result of the rhythmic activity of the vasomotor centre.

Although their results do not definitely show it, they favor the view that the respiration centre, by irradiation to the vasomotor centre, is, in part at least, responsible for the respiratory changes in the volume of the finger. If the respiratory centre can influence the heart and vasomotor centres one should expect to find the vasomotor centre acting on the respiratory as well as the heart centre; therefore, it is possible that the phenomena known as Cheyne-Stokes respiration may find in this its explanation.

**The Circulation and Œdema of the Brain—The Innervation of the Cerebral Vessels.** Biedl and Reiner<sup>1</sup> conclude from their experimental work that the spontaneous oscillations, which sometimes may be observed in the fulness of the cerebral vessels, are mechanically independent of the oscillations of the pressure in the aorta, which occur mostly at the same time, but are often in the opposite direction. The cause of these oscillations is nervous in origin, but as yet they cannot be produced experimentally. Independently of the aortic pressure the suprarenal extract produces a strong contraction of the cerebral vessels if it be introduced directly into the blood. On the other hand, amyl nitrite causes a decided dilatation, also, independently of the pressure in the aorta. There can be no doubt, therefore, that the cerebral vessels have the power of actively contracting and dilating. In these supposedly vasomotor phenomena it cannot as yet be decided what part the peripheral ends of the nerves of the vessels and what part the contractile substance of the vessels themselves play.

**The Circulation in the Coronary Arteries of the Heart.** Langendorff<sup>2</sup> shows by his experiments on the heart of the cat that the former view is untenable, according to which the entrance of the coronary arteries becomes occluded during the systole. He found that the contraction of the cardiac muscle in the beginning dilates the arterial

<sup>1</sup> Pflüger's Arch. f. d. ges. Phys., Band lxxix., S. 158.

<sup>2</sup> Ibid., Band lxxviii., S. 423.

vessels. During each complete cycle of the heart the current velocity has two maxima: one that corresponds to the first part of the systole and one that occurs in the pause.

**Physiological Heart Poisons.** In connection with his former experimental researches upon the heart and the vascular glands as regulators of its activity, Cyon,<sup>1</sup> in his paper (Part IV.) again shows how justifiable were his doubts as to the absolute independence of the automatism of the heart to the cerebral centres. He demonstrates that the conduction of fresh blood through the vessels of the brain suffices to stimulate the stopping heart of the warm-blooded animal to renewed activity.

**The Velocity of Propagation of the Venous Pulse.** With sensitive instruments Morrow<sup>2</sup> was enabled to study the pulsation in the peripheral veins of dogs, with the following results:

1. The oscillations of pressure occurring in the auricle and the venæ cavæ are propagated centrifugally through the veins of the trunk and of the extremities. Pressure and current, therefore, in the larger veins undergo pulsatory oscillations.

2. The velocity of propagation of the venous pulse varies between 1 and 3 metres per second. This relatively small value (about one-half of that of the arterial pulse wave) finds its cause in the lower pressure in and the greater dilatability of the veins.

3. A direct proportion between pressure and velocity of propagation of the venous pulse could not be established in all cases.

4. The velocity of propagation through the jugular vein is, on the average, greater than that through the vena cava to the crural vein.

**The Physiology and Mechanism of Growth of the Vascular System.** Fuchs<sup>3</sup> has found that all the bloodvessels—the arteries more than the veins—are under a longitudinal tension in the living body, because they contract extensively after their removal from the body. This longitudinal tension was found to be quite different for different arteries. The author believes this difference in tension to be the cause of the difference of velocity of propagation of the pulse wave in the different arteries, such as has been observed by Czernak.

**The Local Circulation of Blood in the Area of Paralyzed Nerves.** With the view of studying the character of the circulation of the blood in areas of the body paralyzed from injury to the nerves, Lapinsky<sup>4</sup> selected for his experiments the frog, the area of the body, the foot; the sciatic nerve was exposed and either ligated or divided. In some instances the anterior roots alone were divided. After the disappearance of the post-operative changes he observed the following

<sup>1</sup> Pflüger's Arch. f. d. ges. Phys., Band lxxvii., S. 405.

<sup>2</sup> Ibid., Band lxxix., S. 442.

<sup>3</sup> Arch. f. Physiologie, 1900, S. 102.

<sup>4</sup> Ibid., Supplement, Band ii., S. 477.

permanent results : The bloodvessels were dilated, the velocity of the blood-current was diminished, and the local blood-pressure was normal or greater than before the operation. At times the blood circulated more quickly in the abnormally dilated vessels and under the increased pressure, and at other times abnormally slowly in the same widely dilated vessels.

**The Effect of Compression on One Lung on Respiratory Gas Exchange.** Twenty years ago Weil and Thoma stated what appeared to be a paradox : that there is an increase in the quantity of air breathed and an increase in the quantity of carbon dioxide exhaled when one lung is rendered artificially inactive. Their experiments, which led to this conclusion, were made on rabbits, the lung in different cases being compressed by the injection of cocoa-butter into the pleural cavity. Harley<sup>1</sup> repeated these experiments on dogs with improved apparatus, controlling them so as to avoid error. He found that when one pleural space is filled up so that the lung on the same side is compressed and only the opposite lung remains active, that this is followed in the majority of cases by a marked increase in the rate of breathing. There is at the same time more air actually breathed per minute by the active lung than was previously breathed by the two lungs together. This increase in the quantity of air breathed is accompanied by an increase in the quantity of oxygen absorbed and of carbon dioxide eliminated by the animal, the two being increased *pari passu*, so that the respiratory quotient, as a rule, is not altered.

The cause of the increase in the amount of oxygen absorbed and carbon dioxide eliminated is not to be explained by the increased rate of respiration alone, since in some of the experiments this increase was not noticeable, and even in those cases in which there was a marked increase in the rate there was not the greatest increase in the gas exchange from the lung. The only explanation, then, of this seemingly paradoxical phenomenon which appeared to be satisfactory is the theory of Bohr, who considers that carbon dioxide is a secretion from the lining cells of the alveoli, and that it acts as a stimulant to its own secretion. If this be so, then when one lung is compressed and rendered functionally inactive, the other lung would have to eliminate from the organism twice as much carbon dioxide as it originally did. In consequence of this the quantity of carbon dioxide in the alveoli in any given time would be double, which amount would act as a stimulus to the secreting cells, causing an increased elimination of carbon dioxide. If this is correct it naturally follows that the increased elimination of carbon dioxide necessitates an increase in the absorption of oxygen.

<sup>1</sup> Journal of Physiology, vol. xxv., p. 33.

**The Exchange of Gases in the Lungs of Men at Different Ages.** Magnus-Levy and Falk<sup>1</sup> have carried out a series of investigations on this subject on sixty-two persons, male and female, ranging in age from two and a half to eighty-six years. All individuals were examined undressed at perfect rest in bed. Their conclusions were as follows: Referred to the unit of weight, the exchange of gases in children is greater than in adults and in proportion as the individual is younger and lighter. In adult persons the exchange of gases is nearly constant, the smaller individual, however, having a greater exchange per kilogramme than the larger one. In very aged persons the gas exchange decreases, being less per kilogramme than in equally heavy younger individuals.

Referred to the unit of body surface, the exchange of gases in adult persons of different weight is approximately equal, being, however, considerably higher in children and lower in old men. In the female sex gas exchange does not fall much, if any, behind that of the male. Adults of either sex show no difference. At the same time the authors prove that that human machine which is built heavier and is capable of doing more work does not need to have a greater metabolism when at rest than one that is less heavily developed.

**The Physiological Action of Morphine and Some of its Derivatives on Respiration.** Impens<sup>2</sup> concludes from an experimental study of morphine, codeine, heroine, dionine, and peronine on rabbits and on man as follows:

1. Of all these substances of the morphine group heroine affects respiration in the smallest dose. Morphine requires a fivefold dose, dionine a twelvefold, codeine a twentyfold dose, to obtain an effect not even quite as great. Peronine has only a small effect even after a thirtyfold dose.

2. The danger in the use of heroine is much less than with other preparations; it is two and a half times greater with morphine, twelve times with dionine, and twenty times with codeine.

3. The action of heroine is much stronger and more reliable. If we put the action of peronine as 1, that of dionine is 1.4, that of codeine 2, that of morphine 2.5, and that of heroine 3.75. Codeine, dionine, and morphine are not very reliable in their action, and in many cases fail altogether.

4. The energy of inspiration and the volume of air breathed are considerably increased by heroine. Morphine, codeine, dionine, and peronine mostly have the opposite effect. This is the most important point in the therapeutic action of these drugs.

<sup>1</sup> Arch. f. Physiologie, Supplement, 1899, Band ii., S. 314.

<sup>2</sup> Pflüger's Arch. f. d. ges. Phys., Band lxxviii., S. 527.



5. Heroine diminishes the consumption of oxygen, which contributes mainly to its sedative action on respiration. Codeine and dionine also, however, increase the consumption of oxygen after first diminishing it for a while. They thus partly disturb the quieting effect which they could have on respiration.

6. Morphine paralyzes the sensibility of the respiratory centre for  $\text{CO}_2$ ; codeine has a similar though weaker effect; dionine, peronine, and heroine do not paralyze this sensibility.

7. Heroine is a specific, energetic sedative of respiration. The rest of this group of drugs have only a weak, inconstant, and secondary influence upon respiration. They must be given in much larger doses, and thus are more dangerous, in spite of their unreliable action.

**The Amount of Carbon Monoxide in Tobacco Smoke.** Analyzing tobacco smoke, Wahl<sup>1</sup> found that the smoke from a pipe contained 0.6 to 2.7 per cent., and the smoke from a cigar from 1 to 7.6 per cent. of carbon monoxide. He further discovered that the carbon monoxide was undoubtedly taken up by the blood, but inasmuch as it was highly diluted it has no injurious consequences of any kind when inhaled for about four hours. What the results might be if the small amount of CO taken up by the smoker were inhaled constantly the author does not attempt to investigate.

## GLANDS.

**The Physiological Effects of Extracts of the Pituitary Body.** Schäfer and Vincent<sup>2</sup> carried out a series of experiments to determine the physiological effects of extracts of the pituitary body, and for this purpose they employed the pituitary of the ox. Their results almost agree with those of other investigators, especially Howell and Oliver and Schäfer. In these experiments the extract was made with the infundibular and not the hypophyseal part of the pituitary body. They found that the intravenous injection of the extract produced, according to its nature, either a marked rise or a marked fall in the blood-pressure. This led to the assumption that the pituitary contains two active substances—one a *pressor*, the other a *depressor*. The former is soluble in salt solution and insoluble in absolute alcohol and ether; the latter is soluble in salt solution, absolute alcohol, and ether. These active substances are not destroyed by boiling and are dialysable.

The pressor substances produce a marked rise of blood-pressure, due to the contraction of the arterioles. This effect is also accompanied by cardiac slowing, probably incidental to the contraction of the arterioles,

<sup>1</sup> Pflüger's Arch. f. d. ges. Phys., Band lxxviii., S. 262.

<sup>2</sup> Journal of Physiology, vol. xxv., p. 87.

but probably to a direct action on the cardiac muscle or its nervous apparatus, since it frequently is obtainable, though to a less extent, after division of the vagi or the administration of atropine. The action of the pressor substance is a prolonged one, and during the period of its action a second dose is inactive or nearly so.

The solution of the depressor substance when injected into the veins causes a marked fall in blood-pressure, which they attribute to a peripheral action upon the musculature of the vascular system. The action of the depressor substance is evanescent and can be repeated at short intervals.

**The Effect of Suprarenal Extract upon Smooth Muscles.** The researches of Oliver and Schäfer, on the one hand, and those of Szymonowicz and Cybulski, on the other, have demonstrated that the intravenous injection of suprarenal extract produces a considerable increase in the blood-pressure, due to a contraction of the muscular walls of the arterioles. Lewandowsky<sup>1</sup> now shows that the smooth muscular fibres of the intestinal canal and of the bladder are not affected by the suprarenal extract, but that the non-striated muscles of the eye and the orbit are affected in the same way as the muscle fibres of the bloodvessels. He further proves that the extract affects the muscle fibres directly and not through the intermediation of the nerves. The moderate effect on the bloodvessels of the eye by local instillation is explained by the assumption of a partial oxidation of the extract before it reaches the vessels. In the present state of knowledge, the author says, we cannot explain the symptoms of Addison's disease by the physiological properties of the extract of the suprarenal bodies alone.

**On the Occurrence of Iodine in the Thymus and Thyroid Glands.** After a careful examination of a number of thymus and thyroid glands, Mendel<sup>2</sup> concludes there is no satisfactory evidence to show that the carefully isolated thymus of man or animals contains iodine; but it often happens that accessory thyroid glands contain considerably more iodine than their size would account for, and sometimes even more than the thyroid proper of the same individual. He confirms the observations that the thyroids of newly born children contain no iodine.

**The Chemistry and Physiology of the Iodine Substance of the Thyroid Glands.** The thyroid gland as an internal secretory organ, secreting a physiological active substance—iodothylin—which in some way assists in the maintenance of the nutrition, has been called in question recently by Blum.<sup>3</sup> In an article published last year this author gives the results of experiments made on dogs. From these he con-

<sup>1</sup> Arch. f. Physiologie, 1899, Heft 3 and 4, S. 360.

<sup>2</sup> American Journal of Physiology, vol. iii., p. 285.

<sup>3</sup> Pflüger's Arch. f. d. ges. Physiologie, Band lxxvii., S. 70.

cludes that iodothyryn as such does not pre-exist in the gland. In his opinion the thyroid gland is a protective organ for the central nervous system, though it does not give this protection by the secretion of an iodine-holding substance—such as he could discover nowhere—but by the withdrawal from the circulating fluid of certain substances detrimental to the ganglion cells. He believes that the thyroid gland possesses substances, probably albuminous in character, which take up from the blood the free poison. The thyreotoxalbumin which is thus produced by the combination of the toxin and the albuminous substance is freed from its poisonous nature by oxidation processes in the gland, as the most important of which he considers its combination with iodine. As an intermediate product there is formed a toxic albuminous substance which is partially saturated with iodine.

These results, however, are so at variance with those of other investigators that they will have to be strongly confirmed before they can be accepted.

### NERVOUS SYSTEM.

**On Some Numerical Comparisons of the Centripetal and Centrifugal Medullated Nerve Fibres Arising in the Spinal Ganglia of the Mammal.** In order to further our knowledge as to whether any fibres end free in the spinal ganglion; whether either any of the cell processes divide in the ganglion or soon after its exit from the same; and whether the central and peripheral processes of any or of all the spinal ganglion cells are unequal in diameter, Dale<sup>1</sup> made comparisons in number and size of the centripetal and centrifugal medullated nerve fibres arising in the spinal ganglion of the cat. Most of the observations were made on the coccygeal nerves. He concludes that in the cat there are constantly a few more medullated fibres in a nerve immediately distal to a spinal ganglion than in the nerve immediately proximal to the ganglion—*i. e.*, in short, there are a few more fibres in the nerve trunk than in the nerve roots. This excess is, on an average, about 0.5 per cent. of the total number of nerve fibres. These results closely resemble those obtained by Hall, Stiénon, and Birge in other animals. The excess of nerve fibres in the trunk is apparently caused by fibres of not more than  $6\mu$  in diameter, which are in all probability medullated nerve fibres that pass to the trunk by way of the gray ramus communicans, and end in connection with the vessels or other tissues of the ganglion. Allowing for these fibres, he finds that the number of fibres close to the ganglion is the same as the number several millimetres from it, both proximately and distally—*i. e.*, none of the medullated fibres given off

<sup>1</sup> Journal of Physiology, vol. xxv., p. 196.

by the ganglion cells end in the nerve or nerve roots close to the ganglion. As to the size, he found more fibres of  $6\mu$  and upward in the anterior root close to the spinal cord than in the anterior root close to the ganglion; in other words, the fibres taper slightly. There was a similar difference between the size of the nerve fibres in the roots and that of those in the trunk.

**The Degeneration and Regeneration of Motor and Sensory Nerve Endings in a Voluntary Muscle.** Huber,<sup>1</sup> in carefully conducted experiments, was able to bring about regeneration of the motor and sensory nerve endings in a voluntary muscle after they had been caused to degenerate by severance from the central nervous system. Moreover, this regeneration of the degenerated portion of the peripheral nerve and its termination seemed to be brought about by the downgrowth of the axis cylinder of the central undegenerated portion of the nerve fibre.

**The Functional Adaptability of Afferent Nerve Fibres.** Budgett and Green<sup>2</sup> furnish a felicitous series of experiments to prove what had been already surmised, namely, that there is no essential difference in the nature of sensory and motor nerve impulses. In this research the left pneumogastric nerve was severed on the cranial side of the ganglion of the trunk, and the peripheral cut end was sutured to the peripheral cut end of the hypoglossal nerve. Two or three months later the left pneumogastric was divided just above the thorax. From fourteen to eighteen days after the second operation the vagus, hypoglossal nerve, and the tongue were excised and the peripheral end of the pneumogastric portion stimulated. The muscles of the left half of the tongue responded with weak tetanic contractions, which in most cases, however, were weak. It was not clear whether the nerve impulses transmitted by these fibres to the tongue were motor or pseudomotor, yet their function was evidently quite different from that which they normally possess.

**The Brain of Hermann von Helmholtz.** It was the privilege of Hansemann<sup>3</sup> to study the development and structural peculiarities of the brain of Helmholtz. In his review he calls attention to the unusual development of those parts which are called the spheres of association, and chief among these the terminal region of Flechsig. He calls attention, however, at once to the fact that a similar development of the gyri can be frequently observed in people with ordinary mental powers, so that the presence of those well-developed gyri does not allow us to assume the existence of a high intelligence. These well-developed parts must also functionate well and be in a condition to be easily excited.

<sup>1</sup> American Journal of Physiology, vol. iii., p. 337.

<sup>2</sup> Ibid., p. 115.

<sup>3</sup> Arch. f. Physiologie, 1899.

Such a condition of increased irritability he assumes for the brain of Helmholtz, who in his youth had a slight hydrocephalus, traces of which could still be found at the section.

**The Position of the Motor Centres in the Cerebral Cortex of Man.**

Bechterew<sup>1</sup> reports in this paper the findings after faradic stimulation of the cerebral cortex in three patients who were trephined in his clinic. Electric stimulation was employed in order to determine precisely the position of the centrum which had to be removed. He concludes :

1. The general arrangement of the motor centres in man, in both central convolutions and the neighboring parts of the frontal convolutions, is quite analogous to the corresponding relations in the monkey.

2. The centres for the lower extremity are found in the upper part of the posterior central gyrus ; the centres for the upper extremity in the median part of both central gyri ; immediately below these centres are those for the thumb and fingers ; the centres for the face have their position in the lower part of the cerebral convolutions.

3. The centres for the lateral movements of the head and the eyes correspond, just as in monkeys, to the posterior part of the second frontal convolution, and probably also in its immediate neighborhood.

4. The centres for the muscles of the body are found on the surface of the anterior central gyri, above the centres for the upper extremity, while, according to the statement of later authors, this centrum in the monkey is said to be situated on the medial surface of the hemisphere corresponding to the upper end of the anterior central convolution. His researches on monkeys, however, make it appear very probable that in these animals also the centrum in question lies on the lateral surface of the hemisphere at the upper part of the anterior central gyri.

5. In man, as well as in monkeys, there are special centres for the movements of the thumb and for the fingers ; these lie in the region of the central gyri below and outward from the motor centres of the upper extremity. As in monkeys, so in man, the special cortical centres are separated by areas that cannot be stimulated by the faradic current.

Bechterew<sup>2</sup> reports in an article entitled "The Sensory Functions of the so-called Motor Zones of the Cerebral Cortex in Man," that he observed in the three cases operated upon distinct disturbances of sensibility. By means of the algesimeter he found in one patient a slight reduction of the sensibility and a distinct diminution of the muscle and pressure sense of the right hand. There was such a disturbance of the stereognostic sense that the patient could not recognize a key or a spoon with his right hand, while he could do so easily with his left hand.

<sup>1</sup> Arch. f. Physiologie, Supplement, 1899, Band ii.

<sup>2</sup> Ibid., 1900, Heft 1 and 2.

**The Auditory Centres of the Cerebral Cortex.** From the experimental work conducted by his pupil Larionow, Bechterew<sup>1</sup> concludes, in accordance with the researches of Munk, that in the dog, at least, there exist in the auditory sphere of the temporal lobe different centres for the different tones; or, in his words, there exists in the cortex of the temporal lobe a similar scale of tones as in the cochlea, and the strings of the cochlea are here represented again by different neighboring groups of nerve cells. He believes that the anatomical and clinical findings in man favor the same arrangement. Dr. Larionow<sup>2</sup> published his researches in this direction under the title "The Musical Centres in the Brain."

**A Case of Word Deafness.** The eminent neurologist, Prof. E. Mendel,<sup>3</sup> describes a case of left-sided hemiparesis, with special affection of the left leg and with hallucinations of smell. Among the psychic symptoms the most prominent was word deafness. The man was right-handed. From the symptoms described Mendel concludes that there was a double-sided cerebral lesion. Such a double affection has been shown by autopsy to exist in several similar cases observed by Wernicke and Friedlander, Pick, Mills, Edgren and others; on the other hand, many cases have been found in which a one-sided cerebral lesion did not produce marked word deafness before death. Mendel, therefore, concludes that only a double-sided affection can produce a complete and lasting word deafness.

### SPECIAL SENSES.

**The Width of the Pupil.** The words of Helmholtz, that the regulation of the width of the pupil possesses in a high degree the character of an organic purpose, have been confirmed by Lans.<sup>4</sup> He found in complete darkness the horizontal diameter of the pupil of his right eye, after complete adaptation, to be 7.8 mm. (Dr. Du Bois Reymond had found under the same conditions a pupillary diameter of 10 mm. when the iris appeared as a narrow rim of 1.5 mm. breadth). He further observed that with increasing intensities of light from 0 to 25 metre candles, and often complete adaptation, the diameter of the pupil decreased, first rapidly and later slowly. The same result was observed with an illumination of 25 to 900 metre candles, and it was also found that this diminution of the pupil took place correspondingly with the increase of visual acuity during increased illumination.

<sup>1</sup> Arch. f. Physiologie, Supplement, Band. ii.

<sup>2</sup> Pflüger's Arch. f. d. ges. Physiologie. Band lxxvi., Heft 11 and 12.

<sup>3</sup> Arch. f. Physiologie, 1899.

<sup>4</sup> Ibid., 1900, Heft 1 and 2, S. 79.

**The Cause of the Physiological Pulsation of the Retinal Veins.**

Turk<sup>1</sup> has studied the relation which exists between the different phases of cardiac activity and the pulsation of the retinal veins in a number of persons in whom the heart-beat was irregular (arhythmia). He observed that on the omission of an arterial pulse wave the papillary veins which had been dilated by the last regular wave now became a little narrower than usual. During the entire period of time corresponding to the absence of the arterial pulse wave the veins remained narrow. From this observation, by which it is proved that the narrowing of the veins is not caused by an increase in intra-ocular tension at the time of the heart systole, and is, indeed, independent of the entrance of the pulse wave into the eye, he infers that the systole of the heart produces not the narrowing, but the dilatation, in the phenomena known as the venous pulsation in the retina.

This pulsatory increase in the intravenous pressure, which must give rise to the dilatation, Turk also shows cannot be caused by a rhythmic interference with the exit of the blood from the vena centralis retinæ, because a dilatation caused in this way ought to be propagated in a direction opposite to that of the blood current. He considers it to be caused, therefore, in the only other way possible, namely, by a propagation of the arterial pulse wave through the capillaries into the veins, which is accounted for by the relatively high extravascular pressure in the eye.

The fact that in spite of the same pressure the choroidal veins do not pulsate can be accounted for by the great anatomical narrowing which the vortex veins undergo in their passage through the sclera.

**Artificially Produced Color Blindness.** After fixation of the eye upon a piece of white paper illuminated by sunlight for about three minutes, Beck<sup>2</sup> found that the power of perceiving red and green became greatly weakened or lost, and especially if the colored objects were viewed in a weaker illumination than that by which the color blindness had been brought on. In this weaker light, red paper, according to its brightness, appeared brown or black, while green appeared gray or black. The perception of yellow, blue, and violet was very slightly, if at all, interfered with. The spectrum of white light appeared shortened to the affected eye. Red, according to the degree of color blindness, was either not visible at all or more or less shortened. Green, also, was either not visible, so that at about the wave length of  $510\lambda$  it changes directly into yellow, or it is seen with great indistinctness. The spectrum appeared shortened also at the

<sup>1</sup> Arch. f. Physiologie, 1899, S. 568.

<sup>2</sup> Pflüger's Arch. f. d. ges. Physiologie, Band lxxvi., S. 634.

violet end. Beck believes that the cause of this phenomenon lies in the unequal fatigue of the retinal elements that have to do with the perception of colors.

**The Optic Projection of the Retinal Meridians upon a Plane Perpendicular to the Visual Line in the Primary Position.** Prof. L. Hermann<sup>1</sup> proves that the torsional angle  $\gamma$  of Helmholtz, between the plane of the horizontal meridian and the visual plane, equals the angle which the vertical arm of the fixed cross makes with the absolutely vertical line on the vertical wall when the after-image of the cross is projected on the wall. It is interesting to note that the same relation had been found and published in this country some months before the appearance of this paper of Hermann's. Dr. Carl Weiland and Dr. G. Hay published their papers, the former in the March number of the *Archives of Ophthalmology*, 1899, and the latter in the *Journal of the Boston Society of Medical Sciences*, October, 1899. Prof. Hermann's paper appeared in November, 1899.

**The Function of the Stapedius Muscle.** From theoretical considerations, as well as from experimental work, Ostman<sup>2</sup> concludes that, at least in the dog, the stapedius muscle contracts during the first moment of reflex listening, and that this contraction, as far as the mechanical function is concerned, can have no other meaning than that the tympanic membrane by a slight relaxation is put into a position highly favorable for the reception of sound, and that the labyrinth, by a diminution of the intralabyrinthine pressure, is better adapted for the reception of sound vibrations. He therefore regards the stapedius muscle as a sort of an accommodation muscle of the ear.

**The Labyrinth of the Ear—Space Sense and Orientation.** Prof. E. v. Cyon<sup>3</sup> confirms his theory of the space sense by various new observations made especially upon dancing mice. He defines his theory as follows:

1. Orientation proper in the three planes of space—*i. e.*, the choice of the directions in space in which the movements are to occur and the co-ordination of innervation centres necessary for the selection and maintenance of these directions is the exclusive function of the semi-circular canals.

2. The regulation of the degree of innervation for these centres, as well as for those which govern the maintenance of equilibrium and other purposive movements, is accomplished by the labyrinth. This regulation is influenced at the same time by other sensitive structures

<sup>1</sup> Pfüger's Arch. f. d. ges. Phys., Band lxxviii., S. 87.

<sup>2</sup> Arch. f. Physiologie, 1899, S. 546.

<sup>3</sup> Pfüger's Arch. f. d. ges. Phys., Band lxxiv., S. 211.



(eye, organs of touch, etc.). In case of absence of the labyrinth such regulation can be supplied more or less completely by these organs.

3. The sensations produced by stimulation of the semicircular canals are sensations of direction and space. These sensations in man form the basis for his idea of a space of three dimensions, upon which he projects the space of sight and touch. Animals with only two pairs of semicircular canals—*e. g.*, *petromyzon fluviatilis*—receive sensations of only two directions and can orient themselves only in these; animals with but one pair of canals (*myxine* and Japanese mice) receive sensations of only one direction and can direct themselves only in this.

**The Physiology of the Larynx.** From experiments made on dogs Kuttner and Katzenstein<sup>1</sup> have come to the conclusion that in man, as well as in the dog, both the adductors and abductors are innervated during quiet and rapid respiration. During inspiration the innervation energy of the abductors increases, during expiration that of the adductors. The movement that is produced by the increase of the active force of one muscle group is increased by the passive relaxation of the other muscle group. All laryngeal pictures observed during respiration rest on this principle. The difference of laryngeal pictures is effected only by the difference in the energy with which the one or the other muscle group is stimulated to activity. Beside the posterior crico-arytenoid muscle, other muscles may also effect an active abduction of the vocal cords. For example, the lateral crico-arytenoid and possibly, also, the transverse arytenoids and the crico-thyroid.

<sup>1</sup> Arch. f. Physiologie, 1899, S. 274.



# HYGIENE.

BY HENRY B. BAKER, M.D.

PROGRESS in hygiene consists in advancement of knowledge (1) of the causation of diseases, (2) of the modes by which communicable diseases are spread, (3) of the modes of entrance into the body of those diseases which are communicable, and (4) of the best measures for the avoidance, for the restriction, and for the prevention of diseases.

## 1. THE CAUSATION OF DISEASES.

**Toxins.** 1. Although for the production of a specific disease the specific cause of that disease must be present in the body, or at least so nearly within the body that the toxin elaborated by the specific cause shall be absorbed into the body, as is the case in diphtheria, in which disease the germs are usually in the throat and the toxin is absorbed from thence into the general circulation; yet it is now known that an abnormal condition—a fever or a paralysis—may be produced at any time by the injection into the body of a toxin, as, for instance, tuberculin or the diphtheria toxin which has been entirely freed from any specific living thing.

2. Again, toxins produced by the life-processes of micro-organisms not yet considered the causes of any specific diseases are now believed under certain circumstances to cause abnormal conditions complicating specific diseases, which conditions are known as “secondary infections,” and, under some conditions, may even rank as named diseases.

3. Finally, numerous toxins are constantly being formed in the body by the physiological activities of the various kinds of cells, so that any stoppage of the excretion of any part of the body results in immediate auto-intoxication, the extent and seriousness of which depend upon the extent and importance of the stoppage.

4. It is an axiom that “a mill-wheel cannot be turned by the water that has passed,” and that back water may stop the turning even by water that has not passed; so, also, functional activities of organisms cannot be maintained on material that has been already thus used, and the waste products of the activities of every cell are toxic to that cell.

5. Another generalization which promises to be useful is that a toxin

formed in one part of the body may exhibit very strong influence in a distant part of the body. The toxins of diphtheria and of tuberculosis are not the only ones which thus act. "That blood infected with a toxin, even partially, will scarcely be apt to produce gastric juices of irreproachable chemical composition is indeed self-evident; but also direct experiences with patients who, from whatever side, were exposed to a septic infection are at hand in sufficient numbers to bear direct testimony that its reaction makes itself felt as early as possible upon the digestion."<sup>1</sup>

According to Ponfick, a large proportion of the sickness of children is caused by toxins absorbed into the general circulating blood from pus which forms in the middle ear because of the entrance of germs through the Eustachian tube from the throat. He expresses the idea that the toxins thus absorbed first interfere with digestion, then with assimilation, and finally with excretion in the intestine, thus deranging the entire alimentary canal. This results from the retention of the pus and the consequent absorption of its toxins. "The reversed experience is not less easily understood, that almost in the same moment where the seat of pus is discharged, also the damaging influence on the whole organism ceases."<sup>2</sup>

6. Whether the result of the injection, the ingestion, or the retention of a toxin shall be a fever, a paralysis, an epileptic, tetanic, puerperal, or other convulsion, a headache, a colic, a gouty pain, or some other abnormality, depends very much upon the nature of the toxin.

In recent times enough has been learned to make further investigations in these directions of great promise, as probably leading to such knowledge of the causation of morbid conditions as to greatly aid in avoiding or preventing disease.

### Diseases Not Known to be Specific, Yet Due to Toxins.

**Neurasthenia.** An important contribution to the study of the causation of neurasthenia, which appears to bear upon the causation of several diseases and morbid states, has been made from the clinical side of medical science. In an address before the Chicago Society of Internal Medicine, March 29, 1900, Dr. McCaskey,<sup>3</sup> of Fort Wayne, Indiana, dealt with the causation of that morbid condition known since Dr. Beard's work, about twenty-five years ago, as neurasthenia. As a result of careful philosophical study of numerous cases in which full diagnoses were made by means of the most approved methods—by quantitative exami-

<sup>1</sup> Berliner klinische Wochenschrift, October, 1897, p. 890.

<sup>2</sup> Ibid., October 11, 1897, p. 891.

<sup>3</sup> Journal of the American Medical Association, June 16, 1900, pp. 1531-35.

nations of the urine for amounts of urea, uric acid, chlorides, phosphates, and sulphates; estimates of indican, phenol, etc.; analysis of stomach contents, etc., and by noting results of treatment, he says: "On thorough disinfection of the stomach and large intestines I have seen the most remarkable and immediate amelioration of symptoms in many cases, and in some many times, where the syndrome was that of a typical neurasthenia. This has occurred so often under my own observation that it amounts, in my mind, to absolute proof of the etiological relation of gastro-intestinal disease to the condition known as neurasthenia. It appears perfectly clear that if these conditions can immediately and unmistakably intensify the symptoms of neurasthenia, with equally immediate amelioration on their correction, then the possibility of such conditions acting as a primary cause is settled beyond a doubt."

The foregoing is under the heading "The Importance of Gastro-intestinal Disease in the Aggravation and Perpetuation of Neurasthenic Symptoms in Cases in which the Neurasthenia is Clearly the Primary Condition." But this is only one of several lines of thought leading Dr. McCaskey to the belief that neurasthenia is caused by toxins from various sources. He does not definitely, as he might, call attention to the fact that every organism in its life-processes evolves a substance or substances poisonous to itself, but that generalization is evidently in his mind. He says:<sup>1</sup> "First in importance is the structural alterations in the ganglionic cells under the influence of overaction or fatigue, and the credit for our knowledge of this belongs to American medicine in the person of Dr. Hodge, whose investigations have been followed by similar work all over the scientific world, culminating in the recent tentative volumes by Barker and Van Huchten. . . . I must content myself by pointing out that it has been satisfactorily proved that there are definite structural alterations of the neuron, as a result of fatigue, which can be positively demonstrated under the microscope by the proper technique. The most constant phenomena observed by different investigators are shrinkage or disappearance from the cell body of certain granular masses variously known as Nissl bodies or tigroid masses, the precise nature, function, and significance of which still remain in doubt. Whatever views may be entertained with reference to the validity and importance of the neuron as an anatomical and physiological unit, they can have no bearing on the authenticity of these observations, and their significance is of equal importance, compared with either the older or the newer conceptions of nerve structure. In close juxtaposition to these observations come those of Nissl, Goldscheider, Dana, Lugaro and others on the effect of various inorganic

<sup>1</sup> Journal of the American Medical Association, June 16, 1900, pp. 1531-35.

and organic toxins on the structure of the cell body in the way of cell atrophy, morbid pigmentation, destruction of tigroid masses, etc.; these, while possibly, but not certainly, varying with the kind of toxin used, bear a general resemblance in character to those produced by excessive fatigue. . . . If it be true that many toxins experimentally introduced into the circulation produce such important modifications in the ganglionic cells of the nervous system, then it is a legitimate inference that some of the toxins generated within the organism may have a similar influence. Indeed, it is not altogether an inference, because in the acute and chronic infections there has already been demonstrated the association of analogous changes in the nervous system. With reference to the acute infections, it has heretofore been held by most observers that they were the result of the high temperatures incident to different morbid processes. Recent investigations have shown that these alterations in the ganglionic cells do not occur in high temperatures experimentally produced unless the latter reach 104° F. or more, strongly indicating that in most cases the cell alterations which are found with much lower temperature are the result of poisons formed within the organism, either in the strict and narrow sense or in the gastro-intestinal tract. . . . Admitting the importance of these autochthonous poisons, we have to consider the accumulation of the chemical products of molecular changes within the cell structure always and everywhere resulting from cell activity, commonly known as function. For obvious reasons, these chemical products and the phenomena of their retention and removal are best understood with reference to the muscle-cell, where they are composed of inorganic compounds—mostly combinations of phosphoric and carbonic acid, the potassium salts of which in excess are certainly toxic—together with many others, organic in character, such as *crusocreatinin*, *pseudoxanthin*, and other *leucomaines*, as well as *inosit* and other non-nitrogenous extractives—all of which play an important, if not the principal, rôle in the complex phenomena of muscle fatigue. The existence of these or analogous chemical products as a result of the functional activity of the ganglionic cells is an incontestable corollary of physiological law; and it is more than probable that the condition of the ganglionic cell in the state of fatigue is such as to seriously impair those molecular changes by means of which it excretes, if I may so express it, its own toxic *débris*, and assimilates in exchange its nutrient supply from the *pabulum* which surrounds it. We have thus, viewing the cell as a unit, what may be justly regarded as a primary auto-intoxication in the strictest sense of the word. Going a step further, we may confidently affirm that under conditions of general fatigue the mechanism of elimination of poisons or their disposal by oxidation or other chemical processes is more or less seriously impaired.”

The subject is sufficiently important in itself to be of great interest ; but, to my mind, the chief interest in the study is on account of its important bearing upon the clinical pictures of nearly every disease, because the influence of the various toxins on nerve action and, conversely, the influence of impaired nerve action on the various life-processes throughout the body are exceedingly important in most diseases ; and in neurasthenia there is the best opportunity to study these influences uncomplicated by others.

**Epilepsy.** The view of Haig, that epileptic fits are dependent upon the fact that the uric acid retained in the system before the paroxysm then passes into the blood, is doubted by Krainsky, who through later researches was "able to confirm the fact that no modification took place in the absolute production of uric acid, but only an irregularity of its excretion. He was able to establish a certain ratio between the lessened daily amount of uric acid excreted, on the one hand, and the intensity and number of the convulsions, on the other hand. It may be assumed that about 0.25 of the uric acid is retained in the system before the paroxysm. As the amount of the retained acid is greater, so will the expected attacks be more severe, and reversely. If, in comparison with the average, more than 0.3 of the uric acid is retained, or if the decrease of the excretion is still more marked on the following day, we may rightly assume that several convulsions, or a very violent single fit, will follow. These facts led Krainsky to the opinion that epilepsy is not to be regarded as a purely nervous disease (we consider now only cases of true epilepsy), but as an anomaly of the metabolism which is caused by the poisoning of the organism by some 'product of metamorphosis.'"

"The pathological product of metabolism, which causes the epileptic attacks and which in turn is destroyed by the seizures, is to be sought for by various means. Krainsky injected 2 c.cm. of defibrinated blood, which had been taken from a patient during the *status epilepticus*, subcutaneously into a rabbit. Two or three minutes after a severe epileptic attack followed, which was accompanied by a cry and especially by clonic spasms lasting about two minutes, whereupon the posterior extremities of the animal appeared paralyzed. In the first four days after the injection ten convulsions occurred, followed by death. In another experiment 1 c.cm. of blood from an epileptic, who suffered from periodical attacks of deep coma which frequently terminated in epileptic convulsions, was subcutaneously injected into a rabbit. After two or three minutes a convulsion, followed by permanent paralysis of the posterior extremities, occurred. In the course of three days five or six very prolonged convulsive paroxysms happened ; death of the animal occurred on the fourth day. Control experiments demonstrated that blood obtained during the intervals of attack had no toxic effect ; that

is, would not induce convulsions ; and blood taken from an epileptic in the epileptic stage producing the attacks immediately caused paralysis of the posterior extremities, after which periodical convulsions followed until the death of the animal occurred in four to eight days. It should be mentioned that these blood toxins can only be doubtfully determined, or not at all, after isolated convulsions or light epileptic symptoms. The convulsions which later follow the injection give rise to the idea that blood taken from an epileptic during the period of severe epileptic status exercises not only a poisonous action in consequence of the toxin it contains, but also possesses the property, when injected into a rabbit, of bringing about a periodical production of the same toxin which was contained in the injected blood ; this action resembles those of ferments.” In order to study the chemical nature of the pathological processes of metabolism upon which the generation of these toxic metabolic products depend, Krainsky studied the conditions under which the production of uric acid took place. He attempted through theoretical means to determine the toxin, and concluded that the accumulation or the production of carbamate of ammonia was the cause of the epileptic paroxysms.<sup>1</sup> The carbamate of ammonia was produced at the expense of that portion of the urea which under normal conditions was necessary to the synthetic production of uric acid. While the carbamate of ammonia remained in the blood it accumulated sufficiently to produce a convulsion. With reference to the works of Hahn, Massen, Nencki, and Pawlow, Krainsky described the following symptoms of poisoning in dogs with calcium and sodium carbamates. The above authors demonstrated that upon the introduction of these salts into the blood there might be observed, first, somnolence with ataxia ; second, excitation, also with ataxia and blindness ; third, catalepsy, with anæsthesia ; fourth, epilepsy ; and fifth, tetanus. Krainsky injected ammonium carbamate into the blood of rabbits with like results. He inferred that the nature of epilepsy lay in the periodical production of ammonium carbamate, which causes the convulsions, and is, during the same, broken down into urea and water. In a later series of experiments Krainsky endeavored through experiments on the blood to establish the theoretically deduced conclusion that the periodical production of ammonium carbamate is the cause of epileptic paroxysms. The more severe the epileptic symptoms are—*i. e.*, the seizures, somnolence, and excitement, especially in *status epilepticus*—the more prominently does the carbamic acid present itself ; and, on the contrary, in the intervallary periods carbamic-acid reactions were very slightly observable, and often

<sup>1</sup> “Acid, Carbamic ( $H_2N.CO.OH$ ), an acid not known in the free state ; its ammonium salt is contained in commercial ammonium carbonate.”—*Gould's Dictionary*.



only traces of it were present (as is the case in healthy individuals); also the ammonium salt was found in the blood of epileptics in great quantities, all the more so when the epileptic symptoms were marked in the case.

"It is these—the first exact investigations—which placed the theory of auto-intoxication on a scientific basis in regard to the pathogeny of epilepsy. . . . The severe general symptoms of the *status epilepticus*—the fever, prostration, as well as a fatal termination—are certainly for the most part to be traced to these toxins. But still another consideration will be justified in reference to the labors of Krainsky. According to an oral communication of this author, it is only possible to confirm by experiments on animals the toxic effect of blood in but a restricted number of cases. It is not yet thoroughly established that in all epileptic seizures the grave changes exhibited of metabolic processes lie at the basis of the synthetic and oxidation processes or whether they are concomitant. Strictly, in reference to his experimental results, follows the conclusion that only a group of epileptics suffer these metabolic disorders. Perhaps broader investigations will show that this group of epileptics will be separated pathologically and therapeutically from other forms of epilepsy."<sup>1</sup>

### Specific Diseases.

It has now come to be well understood that every specific disease—every communicable disease—is due to the introduction into the body of the specific cause of that disease—a microscopical form of animal life like the plasmodium of Laveran, the specific cause of ague, or of vegetable life which is quite commonly denominated the germ of the disease, and which by its life-processes usually forms a toxin which has an influence in creating the disease. Thus tuberculosis is due to the bacillus tuberculosis, and the toxin which it forms is tuberculin; pneumonia is due to one or another pneumococcus; diphtheria to the Klebs-Löffler bacillus; typhoid fever to the Eberth bacillus; the plague to the bacillus discovered in 1894 by Yersin, etc.

Although no very startling advances in this direction have very recently occurred, much has been done to strengthen and support the knowledge previously gained, and much evidence has been collected relative to what appear to be the specific causes of a few diseases, notably those of scarlet fever and yellow fever—diseases long known to be communicable, and, therefore, specific, yet the specific causes of which were not yet demonstrated.

**Scarlet Fever.** In the Report of the Medical Officer of the Local Government Board of Great Britain for 1897–98, Dr. Klein showed

<sup>1</sup> "Epilepsy," by Binswanger, p. 234 et seq.

that the streptococcus scarlatinæ (Klein) or conglomeratus (Kurth) was regularly to be obtained from throats, and sometimes from the nasal discharges, of scarlatinal patients, but was not obtained from the aural discharge. In the report for 1898-99, Dr. M. H. Gordon continues the study, perfects the morphological cultural identification of the streptococcus scarlatinæ, and confirms Dr. Klein's observations. The medical officer<sup>1</sup> says: "The above experience goes to suggest that, as we had begun to suspect, the streptococcus scarlatinæ is present, though not abundantly perhaps in many instances, in the throats of a large proportion of scarlatina patients up to a late stage of their convalescence and even after seeming complete recovery. Whether, however, this streptococcus always maintains in such circumstances its full virulence is open to doubt; indeed, certain physiological tests by Dr. Gordon of this micro-organism when taken from the throats of scarlatina convalescents tend to reassurance in this particular."

**Yellow Fever.** The most painstaking work recently on the etiology of yellow fever is that of Wasdin and Geddings, and they uphold Sanarelli's claim as to the relation of the germ to the disease. The Sanarelli bacillus is found in a much larger percentage of cases than he reported three years ago. Wasdin and Geddings found it practically in all cases in the diagnosis of which they concurred.

## 2. THE SPREADING OF DISEASES.

**Yellow Fever.** Unless the experiments by Wasdin and Geddings are accepted as proving that the bacillus of yellow fever always enters the human body by way of the air-passages, and in no other manner, the mode of spreading and the mode of entry of the disease into the body are among the important practical questions which remain to be answered.

Many years ago it was a common belief of yellow fever experts in the medical profession in New Orleans that yellow fever was most likely to be contracted by a person who slept or remained overnight in a locality where the fever was. This now suggests the possibility of yellow fever being commonly spread by inoculation by some insect, as the mosquito, flea, or bed-bug, or possibly all of those insects. Its spread through the city was said to be as if its specific cause moved along not very swiftly over the ground, and this might be the case if conveyed by such insects as fleas carried by rats and mice. Experiments in this direction might yield valuable results. This mode of

<sup>1</sup> Twenty-eighth Annual Report of the Local Government Board, Supplement, containing the Report of the Medical Officer for 1898 and 1899, p. 46.

spread is consistent with the fact that yellow fever is apparently not spread directly from the patient, and if confined to night-flying mosquitoes, like the *anopheles*, is consistent with the fact previously mentioned, also with the fact that yellow fever does not usually spread in northern latitudes where mosquitoes are not as common as at the South ; also with the fact that frost puts a stop to its spread. In other words, there is some evidence—not, however, conclusive—that yellow fever may be spread in precisely the same way that malarial fever is spread.

**Malarial Fever.** For the purposes of hygiene, the most important recent progress in connection with this disease relates to the propagation and spread of its specific cause. For this progress we are indebted to Dr. Koch and many others, but chiefly to Dr. Ronald Ross, of the British Army, Surgeon-Major, Indian Medical Service. Until twenty years ago the name of this disease was supposed to be correct—that is, in some way, *mal* air was responsible for its causation. In 1880, Laveran described the protozoan parasite in the blood of man which is now known to be the specific cause of the disease. In 1885, Golgi found a similar parasite in the blood of birds suffering from fever. A recent writer<sup>1</sup> gives a brief classification of the protozoan parasites: “The latest authors make two genera:

“1. *Hæmamoebidæ*.

“2. *Hæmomenas*.

“The first genus contains four species ; two of these produce malaria in birds, the other two in man.

“*Hæmamoeba malarix* causes quartan fever.

“*Hæmamoeba vivax* causes tertian fever.

“*Hæmomenas* has but one species—*H. præcox* (*Laverania malarix* of older authors). It causes pernicious autumn malaria in man.”

**THE CYCLE IN MAN AND MOSQUITO.** “The parasites of human malaria exist in the bloodstream at first in the form of amœboid, motile jelly dots. They grow fast, and usually in from one to three days attain full size. They then pass into the spore form as sporocytes and gametocytes. The sporocyte is the asexual form ; it at once begins to form a sort of capsule, in which appear asexual spores. These spores, according to the species, mature in from one to three days. The capsules then burst, the spores fall into the serum, and soon after assume the amœboid form ; they move about in the blood serum until they find a red corpuscle to attack. The bursting of the spore sacks and the storming of the blood-corpuscles by the new generation of protozoans is correlated to the period of recurrence of the fever, and is the cause of the same.

<sup>1</sup> Paper read before the Raleigh Academy of Medicine ; Bulletin of the North Carolina State Board of Health, July, 1900.

"The gametocytes are the sexual form. They do not undergo any further change in the human body except as they may degenerate and die. They may, in this way, circulate in the bloodstream for days and weeks. If a mosquito of the genus *anopheles* sucks the blood of a person in whose bloodstream the gametocytes are circulating, the cysts as soon as they reach the forecrop of the insect burst. The microbe resumes the cycle of its development. Some of the cysts produce male, some female germs. These coalesce, and the result is a new individual or zygote. These grow rapidly, are very active, and repel the attacks of the phagocytes of the human blood in which they were borne into the alimentary tract of the insect. The zygotes soon bore through the stomach walls of the mosquito and fix themselves upon the external surface in the form of oval cells of from 8 to 10 $\mu$  in diameter. These cells subdivide much like the egg of a vertebrate, and eventually form a capsule full of small spores; each capsule, when mature, is 60 to 80 $\mu$  in diameter, and may contain several thousand spores. The whole process from the time the gametocyte enters the body of the insect until the spores are formed is about ten to twelve days in summer; it is longer in cooler weather. These sexual spores are motile and move about until they reach the bloodstream of the insect; in this they are carried into the salivary glands. When such a mosquito bites a person she injects into the wound some of the saliva and with it the spores of the protozoan. These once in the human bloodstream assume the amœboid form from which we started, and so begin a new cycle."

For the restriction and prevention of this disease the problem is how best to break up the cycle of its spread. Much work has been done in an effort to learn whether or not the spread of the disease is always from an infected person. Dr. Koch seems to conclude that this is the fact. The entomologist just quoted says: "Very few mosquitoes live over winter. These few hibernate as adults. It is possible that some of these hibernating mosquitoes harbor the sexual spores of the protozoan, and may be able to start a new epidemic of malaria the succeeding summer; but if this was the only way the protozoans could pass from one warm season to another the disease would die out in many localities. The more common way of passing the cold season by the parasite is as spores in the blood of persons who had acute malaria the preceding summer. . . . If all convalescents from summer or autumn malaria were isolated or treated during the winter with enough quinine or methylene-blue to kill the spores in their bloodstreams the mosquitoes of the next season would find no parasite to disseminate, and malaria must die out.

"Entomologists classify mosquitoes into five genera, of which three are rare and of no economic importance. The remaining genera are

*culex*, of which we have in the United States about twenty-two species. . . . Of *anopheles* we have in the United States only three species so far as known. . . . Entomologists are now busy in most regions where malaria is endemic in studying the species of *anopheles* found therein. So far publications show that this genus is very poor in species, and that the number of individuals belonging to any species of *anopheles* is in any particular region few in comparison with the individuals of the genus *culex*. *Culex* is everywhere the common mosquito. It is concerned in spreading the malarial disease of birds, but so far the parasite of human malaria has not been found in any species of *culex*.”<sup>1</sup>

Many experiments have been made with various substances for destroying mosquitoes and their larvæ; but thus far all methods are too expensive to warrant their general use, so long as knowledge of the habits, times, and places of breeding of the malarial mosquitoes is not yet sufficient to make it possible to formulate economical rules applicable generally for their destruction. For the prevention of their development all collections of stagnant water to which fish have not access should be done away with so far as practicable.

The proof that the specific cause of malarial disease is spread directly by certain species of mosquitoes does not make it certain that it is not sometimes spread in other ways, perhaps indirectly by the mosquito through the drinking water or even through the air. Dr. Richard H. Lewis, Secretary of the North Carolina State Board of Health, suggests that “the connection between drinking water and malarial diseases is so plain and so strong that it simply cannot be ignored or broken. Knowing that the female mosquito—the blood-sucker—laid her eggs on the surface of stagnant water, immediately died, sank to the bottom, and disintegrated, thereby liberating in the water the germs of malaria; and knowing that according to overwhelming evidence persons drinking the water of shallow, open wells are much more subject to malarial diseases than other persons in identically the same environment in every single respect except water, drinking the water of cisterns, driven pumps, or bored wells, we reconcile the two theories by taking it for granted that the malaria-bearing mosquito poisoned in the manner indicated the shallow, open wells.”<sup>2</sup>

**What Has Reduced Malarial Disease?** Up to the year 1884 intermittent fever was the disease which caused most sickness in Michigan; now that disease is rare in Michigan. It may not be possible to accurately apportion the extent of the influence of each change in the con-

<sup>1</sup> Paper read before the Raleigh Academy of Medicine; Bulletin of the North Carolina State Board of Health, July, 1900, p. 44.

<sup>2</sup> Bulletin of the North Carolina State Board of Health, July, 1900, p. 45.

ditions which might have had influence in lessening the disease, but apparently one or all of the following changes should be credited with the improved condition of health: (1) The very general draining of swamps, marshes, and stagnant pools; (2) the general tile underdraining of the soil, thus greatly lessening collections of surface water and making the night air warmer; (3) the general employment of mosquito-nettings, which in late years are made of wire and commonly used in windows and doors during the warm months; (4) without doubt the drinking water has been greatly improved. Possibly it may contain less peroxide of hydrogen than did the water from near the surface, used when malarial disease was prevalent.

During the three years ending with 1879 the average percentage of weekly reports (of representative physicians in active general practice in Michigan) stated the presence of intermittent fever under their observation was 80, while during the three years ending with 1899 the average was only 18 per cent.—less than one-fourth the former prevalence.

Measures which have been so successful in Michigan may not be practicable in every State, but the fact that they have been so successful in Michigan ought to lead to the adoption of similar methods, wherever practicable, in localities where malarial disease still prevails.

### **Principal Modes by Which the Ordinary Communicable Diseases are Spread.**

**Infectious Dust.** Excepting the venereal diseases, which are most often spread by sexual contact by an infected person, most of the ordinary communicable diseases in this country are usually spread by means of infected atmospheric dust. Consumption, diphtheria, pneumonia, influenza, scarlet fever, measles, whooping-cough, and smallpox are usually spread in this manner. Not only are most communicable diseases contracted through the nose or throat, but they are also quite generally spread from the nose and throat. The quantity of air which strikes against the other exposed parts of the body is not much greater than against ordinary surfaces of inorganic substances; but as there passes into the nose about twenty cubic inches of air eighteen times per minute, and so much dust-laden air passes through the nose, much dust is there collected. Generally such dust contains many species of bacteria and spores, and wherever a communicable disease exists dust is apt to contain its germs, some of which are capable of causing a specific disease. The micro-organisms (pus cocci) which ordinarily cause suppuration are so generally present that any break in the skin or mucous membrane is usually followed by the formation of pus. The

germs of pneumonia are quite generally distributed, so that they are sometimes found present in the discharges from noses and mouths of persons not yet suffering from pneumonia. The bacillus tuberculosis is so widely common that a large proportion of all persons sooner or later become infected. Because of these facts, handkerchiefs once used are very liable to spread disease in case any secretion from the nose has dried on, so that it may be detached and form dust that may be taken in with the breath or enter any break in the skin.

Although, for reasons just stated, the nose is the place most liable to gather infections, the mouth also is, to a considerable extent, liable to do so; and when once infectious germs have passed the nose and found lodgement in the body the sputum is very liable to contain them. At the present time all sputum should be considered as probably infectious, and certainly so if any pus is present; and whenever any dangerous communicable disease is in the vicinity the discharges from the nose of every person exposed to the disease are liable to be infected with the germs of that disease.

**Infectious Spray.** Within a year or two Flügge has called attention to the fact that there is another mode of spreading tuberculosis—and probably the same is true of several other diseases, such as influenza, pneumonia, pneumonic plague, diphtheria, etc.—namely, by means of little droplets of saliva or fine, moist spray thrown out from the mouth in coughing, sneezing, and even in ordinary speaking.

“From examinations made by Laschtsenko it is known that the secretion in the mouths of consumptives may contain tubercle bacilli. On swabbing the mucous membrane of the cheek and gums he found that nine out of twenty patients harbored in their mouths tubercle bacilli, and that these were present at times in enormous numbers. On exposing a series of glass slides before consumptive patients it was found that during coughing or sneezing they ejected minute particles of saliva which settled upon the slides. Four out of twenty-one patients were thus shown to scatter tubercle bacilli. In a still more conclusive manner he showed that the ejected droplets of saliva contained virulent tubercle bacilli. For this purpose the patient was placed in a small compartment, and a number of Petri dishes containing sterile salt solution were arranged at a distance of from three to six feet. After the patient had coughed for an hour or two the contents of the dishes were combined and injected into a guinea-pig. In four out of nine experiments the inoculated animals died of tuberculosis, thus effectually demonstrating the dangerous character of these fine particles.

“More recently Heymann has repeated very carefully the work done by Laschtsenko, and has obtained the same, if not even more striking, results. Of thirty-five consumptives who were caused to cough over

exposed glass slides, fourteen (40 per cent.) were found to scatter droplets containing tubercle bacilli, and in more than one-half of these the bacilli were present in enormous numbers. The further fact that six out of twenty-five guinea-pigs developed inhalation tuberculosis after having been exposed to the cough of consumptives indicates that there is real danger in these sputum particles.

"Actual experiment has shown that lepers in coughing expel in such droplets enormous numbers of leprosy bacilli."<sup>1</sup>

**Transference by Rats.** All observers agree that the plague is in some manner not infrequently transported by rats. It seems probable that the fleas which are commonly on the rats aid in spreading the disease. "In a few cases proof has been forthcoming that persons have contracted plague from the bites of rats."

**Transference by Insects.** Evidence has been accumulating that flies, by means of their feet, are capable of transferring the specific causes of diseases from sputa, excreta, sores, etc., to wounds and to articles of food which, if not afterward cooked, may convey disease to persons who eat them.

**Inoculation.** The list of the diseases conveyed by the bites of insects is increasing. Malarial fever and plague are the most important of such diseases. That malarial fever is conveyed by inoculation by a species of mosquito is now established; that it is exclusively so conveyed is still disputed. Speaking of the effort to restrict the plague, "a crusade which it is quite as necessary should be instituted as the crusade against rats is that against vermin—fleas and bugs particularly."<sup>2</sup>

Probably all communicable diseases may be contracted by inoculation, but some diseases are seldom contracted in any other manner; tetanus is an example. "Recent investigations on protozoal diseases have revealed the fact that several of these are exclusively inoculation diseases, and that such inoculation is brought about directly by the bite or sting of insects. The first really exact work in this direction was made in 1893 in connection with the cattle disease known as Texas fever. It was shown that in all probability the disease was exclusively transmitted through the agency of the tick which infests cattle. The cause of this disease is an animal organism which, like that of malaria, is found within the blood-corpuscles of the diseased animal."<sup>3</sup>

<sup>1</sup> Novy. Proceedings of the Fourth General Conference of the Michigan Health Officials, 1899.

<sup>2</sup> G. J. Blackmore, Late Special Plague Medical Officer, Bombay and Calcutta; *Lancet*, London, June 23, 1900, pp. 1790 and 1791.

<sup>3</sup> Novy. Proceedings of the Fourth General Conference of the Michigan Health Officials, 1899.



### 3. PRINCIPAL MODES BY WHICH THE ORDINARY COMMUNICABLE DISEASES ARE CONTRACTED.

**By Inhalation.** Probably most diseases are usually contracted through some break in the skin or in the mucous membrane lining some cavity, and most of them are apparently usually contracted by taking in the germs with the breath through the mouth, and probably sometimes through the nose. The nose is so constructed and so guarded by minute hairs, kept moist by the exhaled breath and by secretions, that very small quantities of dust or moist particles of any kind are permitted to pass beyond the nose so long as that organ is in its normal condition; but minute breaks, inflammations, or ulcerations occur not infrequently in the throat at those seasons of the year when the atmosphere is what is known as "raw"—that is, when it contains the throat-irritant ozone and when it is irritating by reason of its drying effect in cold, windy weather—and at such times the normal protective condition of the nose is not always maintained.

Few persons have a correct idea of the conclusiveness of the evidence on this subject, for the reason that the evidence can be collected only where reliable statistics of sickness are available for comparison. By such statistics it has been proved, in Michigan, that the prevalence of several diseases which enter the body by way of the air-passages is almost absolutely controlled by the atmospheric temperature.

It is plain that every one of these diseases is almost exactly quantitatively related to the atmospheric temperature—every one of them increases in prevalence after the temperature falls, and decreases in prevalence after the temperature rises.

**By Ingestion.** For a considerable time it has been understood that tuberculosis sometimes gains entrance to the body with infected food ingested, and typhoid fever with infected water drank. Lately evidence has accumulated that typhoid fever sometimes enters with the solid ingesta, the germs having been transferred by the feet of flies from infected discharges to bread and other articles of food taken without further cooking.

**By Way of the Eyes.** One other mode of entrance of pathogenic bacteria cannot be ignored, namely, by way of the eyes, which, although constantly moistened with an antiseptic fluid which washes the dust off and delivers it through the lacrymal canaliculi and nasal ducts into the nose, that fluid must have its limitations as to the numbers of such pathogenic bacteria which it is possible for it to cope with successfully, and in this way invading germs are delivered into the nose above the protections at its entrance. The early sign of measles—the catarrhal in-

flammation of the conjunctiva—is very suggestive of this mode of entrance, and the early signs of influenza are sometimes such as to suggest this mode of entrance of that disease.

**Infectious Diseases are Distributed from the Throat.** Excluding malarial fever and other diseases which enter the body by inoculation, the specific causes of most of the communicable diseases prevalent in this country enter by way of the eyes, nose, and mouth, and are distributed from the throat to the various parts of the body which are to be the sites of their reproduction or lodgement. In any given instance just what part of the body shall then be invaded depends greatly upon conditions existing at the time the throat is reached. If the cilia in the air-passages are paralyzed by cold or by corrosive vapor, such as ammonia, chlorine, or ozone, micro-organisms may readily pass down the trachea—bronchitis or pneumonia may result. If all the defences to the air-passages are in the best condition to resist the entry of pathogenic micro-organisms—as they are, as a rule, in the warmest season of the year—the distribution from the throat is restricted to that extent; but there is then no restriction of the movement of the germs down the alimentary canal, and such as can pass the ordeal in the stomach may cause disease in the intestines. Thus cold weather results in inflammations of the air-passages and lungs, while hot weather results in inflammations in the alimentary canal; and, at any season of the year, such as can enter the general circulation can cause disease in any part of the body where the conditions are favorable.

**In Cold Weather and in Warm Weather Most Infectious Diseases which Reach the Throat Generally Pass on to the Middle Ear.** This very important generalization can now be made, mainly through attention attracted to the subject by Ponfick, of Breslau, although many others have contributed to this result since 1859.

“In Rotch’s *Pediatrics* we read that Von Tröltzsch found, on examining forty-seven petrous bones taken from unselected children, that the middle ear was normal in only eighteen. The other twenty-nine ears showed in varying degrees purulent and sometimes mucous catarrh.”<sup>1</sup>

“Already as far back as 1859 Tröltzsch<sup>2</sup> reported that in twenty-five autopsies on babies he found otitis media present fifteen times. In 1868, Wrede<sup>3</sup> reported from the Foundling Asylum at St. Petersburg that in eighty autopsies there were pathogenic changes of the ear in 84 per cent, and Kutscharianz<sup>4</sup> soon followed with reports from the Foundling

<sup>1</sup> Otitis Media as a Complication in Infectious Diseases of Infancy. By E. H. Pomeroy, M.D., Calumet, Mich. Address before the Upper Peninsula Medical Society, July, 1899.

<sup>2</sup> Verhandlungen der Physik.-med. Gessellschaft zu Würzburg, 1859.

<sup>3</sup> Monatsschrift f. Ohrenheilkunde, 1868.

<sup>4</sup> Archiv f. Ohrenheilkunde, Bd. x., p. 119.

Asylum of Moscow, stating that in 300 autopsies only seventy children showed normal conditions of the ear. . . . In twenty autopsies of infants, Netter,<sup>1</sup> of Paris, found true pathological changes in the ears of each and every case. Kossel<sup>2</sup> reported from Koch's institute in Berlin that in 108 autopsies there was in the ears of eighty-five infants true otitis media containing bacteria mostly of the same kind which were found in the main disease of which the child died."<sup>3</sup>

#### **Otitis Media and the Causation of Gastro-intestinal Disease.**

Ponfick observed in several of his own children that intestinal disturbances arose without the least change having taken place in either food or attendance. He set himself to study whether the trouble was really what it appeared—"essential" gastro-enteritis—or whether it was due to some other cause. He decided that the sickness was not "essential" gastro-enteritis. One sick girl being under observation, the phenomena accompanying the intestinal disturbances remained for four days, when light was thrown on the cause of the child's sickness. It was noticed that irritation of the region of the ear resulted from very light touching of that organ; also, the child showed unmistakably that there was pain in its ear. After investigations Ponfick decided that the seat of the entire sickness was in the middle ear. Then an opening of the tympanum took place, and after a few days the bowel discharges became normal.

Ponfick then sought to gain an adequate number of observations on the relation of otitis to other diseases; so he investigated and reported on the first one hundred post-mortem examinations of children, mostly polyclinical patients, up to and including the first four years of life, taken together in the accidental succession and with the desired diseases exactly as they were admitted to the hospital. The result was that 91 per cent. of the children were found to have had otitis media; only 9 per cent. of the children maintained a normal condition of the tympanum. The shortest way to state all the facts is by means of the table by which Ponfick states them, as follows:

<sup>1</sup> *Comptes-rendus de la Société de Biologie*, 1889.

<sup>2</sup> *Charité Annalen*, Bd. xviii., p. 497.

<sup>3</sup> Otitis Media and Earache in Lobar Pneumonia of Children. J. S. Meltzer, M.D., Association of American Physicians, Washington, D. C., May 3, 1899; Philadelphia Medical Journal, August 5, 1899.

**OTITIS MEDIA IN 100 CHILDREN DEAD FROM THE CHOSEN DISEASES,  
ONE MONTH TO FOUR YEARS OLD.**

|                                                                                   | None. | One-sided. | Double-sided. | None. | One-sided. | Double-sided. |
|-----------------------------------------------------------------------------------|-------|------------|---------------|-------|------------|---------------|
| <b>I. NON-INFECTIOUS PROCESSES.</b>                                               |       |            |               |       |            |               |
| 1. Hereditary heart failure . . . . .                                             | 1     | ...        | 1             |       |            |               |
| 2. Fatal burns . . . . .                                                          | ...   | ...        | 1             |       |            |               |
| 3. Other kinds of dermatitis . . . . .                                            | ...   | 1          | 2             | 1     | 1          | 4             |
| <b>II. INFECTIOUS PROCESSES.</b>                                                  |       |            |               |       |            |               |
| <b>A. Acute.</b>                                                                  |       |            |               |       |            |               |
| 1. Infectious dermatitis . . . . .                                                | 1     | ...        | 3             |       |            |               |
| 2. Diphtheria . . . . .                                                           | 3     | 1          | 2             | 1     | ...        | 3             |
| 3. Scarlet fever . . . . .                                                        | ...   | ...        | 1             | 3     | 1          | 3             |
| 4. Pneumonia . . . . .                                                            | 1     | ...        | 10            |       |            |               |
| 5. Purulent meningitis (with or without pneumonia) . . . . .                      | ...   | ...        | 8             | 1     | ...        | 18            |
| 6. Gastro-enteritis, acute . . . . .                                              | 1     | 2          | 5             |       |            |               |
| 7. Gastro-enteritis, chronic (with or without pneumonia) . . . . .                | 1     | 5          | 21            | 2     | 7          | 26            |
| 8. Otitis media alone . . . . .                                                   | ...   | 2          | 6             |       |            |               |
| 9. Otitis media with acute bronchitis . . . . .                                   | ...   | ...        | 2             | ...   | 2          | 8             |
| <b>B. Chronic.</b>                                                                |       |            |               |       |            |               |
| 10. Tuberculosis, purely chronic . . . . .                                        | ...   | 1          | 3             |       |            |               |
| Tuberculosis, with acute generalization ("acute military tuberculosis") . . . . . | 1     | 1          | 10            | 1     | 2          | 13            |
| 11. Congenital syphilis . . . . .                                                 | ...   | ...        | 3             | ...   | ...        | 3             |
|                                                                                   | 9     | 13         | 78            | 9     | 13         | 78            |

These observations should not be ignored by clinicians; they have an important interest in connection with vital statistics, and they must be considered by those who are studying the causation of disease with reference to its avoidance, restriction, or prevention.

**The Size of and Course Taken by Pathogenic Micro-organisms and the Period of Incubation.** The main reason for the long period of incubation in such diseases as smallpox, in which the infection is not local, as in diphtheria, but general, is probably because of the course by which the pathogenic germs gain entrance to the general circulation. It must be seldom that they go at once into a bloodvessel capable of delivering any considerable number of them into the general circulation; but, as a rule, probably they first enter the lymph spaces and pass through into the veins or are taken up by the lymphatic system and delivered into the general circulation by way of either the right lymphatic duct or the thoracic duct. Although the germs of some diseases, notably syphilis and the plague, and possibly cancer, are liable to

be stopped temporarily at the first lymphatic glands, apparently this is not true of many diseases; and in this is a hint as to the sizes of germs to be looked for. Speaking of the recently discovered germ of pleuropneumonia, Professor Novy<sup>1</sup> has said: "Some idea may be gained of its size when it is said that a magnification of 2000 diameters is not sufficient to reveal the form of the organism. . . . It is not improbable that in vaccine, smallpox, hydrophobia, and in other diseases in which the cause is still unknown, improved methods of study will reveal the presence of similar diminutive microbes."

#### **4. BEST MEASURES FOR THE AVOIDANCE, FOR THE RESTRICTION, AND FOR THE PREVENTION OF DISEASES.**

**Disinfection.** In measures for the restriction of disease one of the most important items of recent progress is the gradual development of practical methods for the employment of formaldehyde as a disinfectant.

One of the first proposals was to generate the gas as it was wanted. This was attempted by the partial oxidation of wood alcohol; but it was found that it was not possible to make sure whether all of the alcohol used was actually so oxidized as to be formaldehyde or whether some portion of the alcohol was simply vaporized; therefore, now that method is abandoned.

Some of the plans for the ready liberation of a known quantity of the gas involved the use of expensive apparatus for the vaporizing of formaldehyde from the solidified formaldehyde—paraform.

It has now come to be known that no very expensive apparatus is required; in fact, it is claimed that a cotton sheet or sheets hung in a room and the 40 per cent. solution of formaldehyde rapidly sprinkled on the sheets from an ordinary sprinkling-pot is all the apparatus actually required; but by this method all the arrangements must have been completed before the sprinkling begins, for the reason that the evolution of the stifling gas is so rapid that the operator must hasten to get out of the room.

For effective disinfection about eight ounces of the 40 per cent. solution should be used for each 1000 cubic feet of space in the room. Articles to be disinfected must be spread out as much as possible, in order to expose all surfaces which need disinfection, as it is not claimed that formaldehyde has great penetrating power.

Professor Novy has recommended the use of a still in which the 40 per cent. solution is placed and vaporized by a blast lamp, the vapor being delivered through a tube from the top of the still through the

<sup>1</sup> Fourth General Conference of the Michigan Health Officials, 1899.

keyhole into the room. In this way a known quantity of the solution can be vaporized into the room while the operator remains on the outside.

One great advantage of formaldehyde over sulphur is that it does not destroy goods by bleaching, as sulphur fumes do, and it does not injure any metallic substance except iron.

For the disinfection of books and mail-matter formaldehyde is much more convenient and safe to use than is burning sulphur; but for such use, where infected surfaces may be covered, it is probably not safe to rely upon so small an amount as eight ounces to the 1000 cubic feet of space.

**PREVENTION OF PLAGUE.** In summarizing notes on the introduction and spread of plague, G. J. Blackmore,<sup>1</sup> late special plague medical officer, Bombay and Calcutta, says: "If plague is to be prevented from entering this country there must be (1) a most careful search made for modified cases of plague for some considerable time after the disease has apparently died out in places that have been attacked by it; (2) rigid inspection of vessels and passengers coming from infected places, not only while they are known to be infected, but for months afterward; (3) disinfection of dirty clothing and rags coming from such places; (4) a sharp lookout kept for any increased mortality among rats in seaport towns, with repeated search for the plague bacillus in the bodies of those found dead; (5) an attempt made to exterminate the vermin which may act as carriers of the plague; and (6) early inoculation of the people when plague has appeared among rats."

The foregoing, written with reference to England, is just as applicable to the United States.

<sup>1</sup> *Lancet*, London, June 23, 1900, p. 1791.

# PRACTICAL THERAPEUTIC REFERENDUM.

By E. Q. THORNTON, M.D.

**Acoin.** This new local anæsthetic was discovered by Trolldenier, of Dresden, who, in his experiments upon dogs, found it to be less toxic than cocaine. It is a white, crystalline substance, soluble in water (1: 8), derived from guanin—a substance found in the cellular tissue of almost all animals and vegetables. It is closely related to caffeine and theobromine. Chemically, it is di-para-anisyl-mono-phen-ethyl-guanidinchlor-hydrate. Dr. R. L. Randolph<sup>1</sup> first experimented with a 1: 3000 solution upon the human eye, for the purpose of extracting foreign bodies from the cornea. In those cases where the foreign body had been embedded for some time and there was congestion, repeated instillations were necessary to make the removal possible, and it was thought that anæsthesia was not as complete as when cocaine or eucaine was used. In cases without congestion no pain was experienced by the patient. He also used the remedy for the removal of pterygium, and two cases of tarsal tumors were opened and curetted with about as little pain as is commonly experienced when cocaine or holocaine is employed. The stinging sensation produced by acoin is greater than that produced by cocaine, and was proven by dropping cocaine into one eye and acoin into the other. In other cases he employed stronger solutions, and concludes that acoin in solution of 1: 100 and 1: 300 produces satisfactory anæsthesia in non-irritated eyes in about the same length of time as cocaine, and that the drug had no effect upon accommodation or upon the size of the pupil, and that it did not increase intra-ocular tension. In several cases where the eye was congested repeated instillations of acoin failed to produce satisfactory anæsthesia.

Brudenell Carter,<sup>2</sup> in speaking of the value of subconjunctival injections in ophthalmic therapeutics, says that on account of the pain produced by such injections, which is always considerable and sometimes very severe, they are resorted to less frequently than circumstances would justify. His attention having been called to the new anæsthetic—acoin—by Darier,<sup>3</sup> who stated it to be non-toxic and capable of producing anæsthesia of long duration, he was led to employ it in a number of

<sup>1</sup> Ophthalmic Record, August 29, 1899.

<sup>2</sup> Lancet, October 21, 1899.

<sup>3</sup> La Clinique Ophthalmologique, June 25, 1899.

cases for the subconjunctival injections, using a mixture composed of equal parts of a solution of cyanuret of mercury of the strength of 1:1000 and a solution of aconitine of 1:100 in normal saline solution. The conjunctiva was cocaineized before the injection was made, and the strictest antiseptic precautions were taken. No pain whatever was experienced by the patient, and the only discomfort was a sense of weight and inconvenience from the swelling which occurred, but which passed away in a short time. He was well satisfied with the anæsthetic, which enables the ophthalmic surgeon to employ a method whose only serious objection heretofore has been the pain produced by its application. For instillation into the eye the following prescription may be employed :

|                           |        |            |
|---------------------------|--------|------------|
| R.—Aconit . . . . .       | gr. j. | gm. 0.065  |
| Aquæ destillatæ . . . . . | f ʒ v. | c.c. 20.00 |

For hypodermatic injection the following solution may be found convenient :

|                           |         |            |
|---------------------------|---------|------------|
| R.—Aconit . . . . .       | grs. v. | gm. 0.32   |
| Sodii chloridi . . . . .  | grs. v. | gm. 0.32   |
| Aquæ destillatæ . . . . . | f ʒ j.  | c.c. 30.00 |

**Airol.** Airol, or bismuth-oxy-iodo-gallate, is a greenish-gray, odorless and tasteless powder. It is insoluble in water and alcohol, but is dissolved in glycerin, weak alkalies, and weak acids. When brought in contact with wounds it is decomposed by the serum of the blood, with the liberation of iodine. It has been used internally as an antiseptic and intestinal astringent, and locally in the form of a dusting-powder or ointment as a substitute for iodoform. The dose of airol is from 5 to 10 grains (0.32 to 0.60 gramme), repeated at intervals of three or four hours. Taussig employed the following formula as an injection in the treatment of gonorrhœa :

|                     |          |           |
|---------------------|----------|-----------|
| R.—Airol . . . . .  | ʒ ijss.  | gm. 10.00 |
| Glycerinæ . . . . . | f ʒ jss. | gm. 45.00 |
| Aquæ dest. . . . .  | f ʒ jss. | gm. 45.00 |

Doederlein<sup>1</sup> and Fränkl<sup>2</sup> have employed the ointment after closure of abdominal and perineal incisions, to prevent suppuration from the stitches. Fränkl prefers the dry powder or airol gauze to the ointment as a dressing.

**Amylene Hydrate.** Amylene hydrate, or tertiary amylic alcohol, is a colorless, hygroscopic liquid, with a peculiar camphoraceous odor. It is soluble in water (1:8), is freely miscible with alcohol, ether, glycerin, and fatty oils. Its dose as a hypnotic is from 15 to 60 minims (1 to 4 grammes). On account of its disagreeable taste, the best method

<sup>1</sup> Centralblatt f. Gynäk., July 7, 1900.

<sup>2</sup> Ibid., June 2, 1900.



of administering it is in soft capsules. W. Niessen<sup>1</sup> employed the drug extensively in the treatment of diabetes insipidus. In many cases there was temporary improvement in the polyuria and polydipsia, and in some cases permanent cures were effected.

|                            |     |           |
|----------------------------|-----|-----------|
| R.—Amylen. hydrat. . . . . | 3j. | c.c. 4.00 |
| Olei menthæ virid. . . . . | ℥j. | c.c. 0.06 |

Misce et pone in capsulas No. iv.

Sig.—One to two capsules at bedtime.

For whooping-cough for a child of four to six years :

|                             |            |            |
|-----------------------------|------------|------------|
| R.—Amylen. hydrat. . . . .  | 3j.        | c.c. 4.00  |
| Tinct. belladonnæ . . . . . | gtt. xxiv. | c.c. 1.00  |
| Elix. aromat. . . . .       | f℥iij.     | c.c. 90.00 |

Misce. Sig.—Teaspoonful every five hours.

**Antipneumococcus Serum.** In dealing with pneumonia we are confronted not only with the difficulty of antidoting the (undiscovered) toxin in the blood, but also the difficulties of dealing with a disease in which there is a general tendency to septicæmia and extensive exudate within the lungs. The antipneumococcus serum, as now prepared, is neither bactericidal nor antitoxic, but its usefulness, so far as laboratory experiments can prove, is entirely confined to prevention or modification of the septicæmic process. In other words, the value of the serum appears to depend upon its power to so alter the pneumococci as to render them easy victims to the phagocytes. The Italian clinicians appear to have obtained better results from the use of the serum than by the usual methods employed ; but elsewhere, except in isolated instances, the results have been far from satisfactory.<sup>2</sup>

Alexander Lambert<sup>3</sup> has given up the use of antipneumotoxin in the treatment of pneumonia, as it did not appear to shorten the duration of the disease nor cut short the pneumonic process in the lung, nor did it bring about the desired crisis. In the twelve cases reported by him, in which he employed a serum prepared by himself from the blood of an immunized horse, there were three deaths and nine recoveries. He states that some of the cases were undoubtedly benefited, although upon others there was no effect whatever. Only in one case was leucocytosis influenced. In this case the increase of leucocytes was 10,000 an hour after the injection, but fell the following day. Charles B. Canby<sup>4</sup> reports four cases of pneumonia of usual severity successfully treated with Pane's antipneumotoxin. In all of the cases the temperature declined, respiration became less frequent, and in all but one the pulse-rate was

<sup>1</sup> Therap. Monatsheft, August, 1900.

<sup>2</sup> See PROGRESSIVE MEDICINE, 1900, Vol. III., p. 49.

<sup>3</sup> Journal of the American Medical Association, April 14, 1900.

<sup>4</sup> Maryland Medical Journal, March, 1900.

reduced. In one case there was a relapse, which was promptly controlled by again resorting to the serum. The serum most generally employed is that of Pane, prepared from the blood of turkeys. Its dose is from 10 to 20 c.c. ( $2\frac{1}{2}$  to 5 drachms) at a single injection, to be repeated once or twice daily. Although many observers have failed to obtain satisfactory curative results, we have yet to see a report of any ill effects following its use, and would be inclined to employ it in conjunction with the usual remedies in severe cases.

**Antitubercle Serum.** The serum obtained from the blood of animals treated with the toxins of the tubercle bacillus should not be confused with tuberculins and other products of bacterial growth. Dr. J. Edward Stubbert, of Liberty, New York, in a paper read at the annual meeting of the Climatological Society in 1898, reported a series of cases of incipient pulmonary phthisis in which by climatic, hygienic, dietetic, and serum treatment 39 per cent. had been apparently cured and 55 per cent. generally improved, and in 9 per cent. of the latter cases the disease had been arrested. In a recent paper<sup>1</sup> he described the present condition of these cases, classifying them into those who had been away from the sanitarium for three years and those who had been away for two years. There was a total of fourteen patients comprising this 39 per cent. He was able to trace and obtain accurate histories of nine of these, and from general repute learned that the other five were in the same condition as when discharged from the institution. Of the nine of whom accurate histories were obtained up to date four had been away from the sanitarium for three years and five had been away for two years. None had relapsed, and all were attending to their usual duties under ordinary conditions. All of the cases reported were selected cases, and no claim is made for the serum alone, but the results have been brought about by combining its use with hygienic and climatic treatment. He also reported nine other incipient cases, who after a year's absence from the institution are apparently cured, and also three cases in which the active process has been arrested and the patients enabled to return to their work in their old environments.

Paquin<sup>2</sup> does not believe the serum treatment is indicated in all cases of tuberculosis, but thinks that many incipient cases may be benefited. In cases with albumin in the urine and also where there is cardiac insufficiency, caution in dosage should be observed. There is a great difference in the individual's susceptibility, and small doses should be employed at the beginning. Thirty drops a day, given six times a week, is sufficient after tolerance is established. The treatment should be interrupted one week in six, and when again renewing it small

<sup>1</sup> Medical News, August 18, 1900.

<sup>2</sup> Medical Mirror, March, 1900.

doses should be employed at first. In some patients slight eruptions and flushings are observed, and in these the treatment should be temporarily discontinued. The best results are to be obtained only when the patient's hygienic and dietetic surroundings are carefully regulated and he is given the advantages of climatic treatment. He permits the use of the serum by injection into the bowel in some cases, and the dose should be twice as great as when used by the hypodermatic method.

E. A. de Schweinitz<sup>1</sup> has prepared serum from the blood of horses injected with a solution of germ poisons as free as possible from the fatty matter of the germ. Only after several years of treatment did the serum from such animals show neutralizing and curative properties. He considers the results of the trials by Stubbert in the Loomis Sanitarium encouraging.

**Antivenomous Serum.** There can be no doubt that Calmette's serum is the most valuable remedy known for the treatment of bites from poisonous snakes and scorpions. Abundant evidence of this fact is to be gathered from the reports of a great number of English physicians serving in the English army in India, and I have not been able to find an instance in which this serum was employed where death resulted from the bites of the most venomous reptiles. This antidote consists of the serum obtained from the blood of horses which have been rendered immune to the action of gradually increasing doses of mixtures of several of the most poisonous snakes of India. The method of procedure, according to O. O. Andrews,<sup>2</sup> is as follows: Three grammes (48 grains) of dried venom obtained from three distinct species of snakes (*Crotalus durissus*, *Bothrops lanceolatus*, and *Naja tripudians*) and of viperine and columbine are dissolved in 300 c.c. (10 ounces) of distilled water, occasionally agitated, for twenty-four hours. Equal quantities are then poured into three flasks and heated for thirty minutes in a water-bath at a temperature of about 72° C. It is then filtered through white filter-paper to remove the white, flocculent precipitate which settles to the bottom. A strong, healthy horse is selected and is proved to be free from glanders by the use of the mallein test. The neck, after being thoroughly cleansed, is washed with a carbolic solution, and half a milligramme ( $\frac{1}{125}$  grain) of venom (0.5 c.c. of 1:100 solution) is injected into the subcutaneous tissues in front of the shoulder. In a few days the abscess which forms as a result of this injection is opened and dressed with an antiseptic solution. Fifteen days later, if the abscess is healed, 1 milligramme (1 c.c. of solution) is injected. In fifteen days more 2 milligrammes are injected. Increasing doses are administered from time to time, so that at

<sup>1</sup> Journal of the American Medical Association, April 14, 1900.

<sup>2</sup> British Medical Journal, September 9, 1899.

the expiration of one year the animal is able to resist 500 milligrammes (50 c.c. of solution). After sixteen months of treatment the animal should be sufficiently immunized to resist 1 gramme (100 c.c. of solution) of the poison. The serum from an animal thus immunized is capable of yielding serum of the strength of 200,000 units. Immunity in animals produced by this method is comparatively evanescent, and in order to keep up the immunity to the maximum degree of resistance 1 gramme is put in 100 c.c. of solution and injected every two or three months. When it is desired to obtain serum the horse is bled in a manner similar to that employed in obtaining antidiphtheritic serum. The blood is placed in a dark, cool room for twenty-four hours, to permit the serum to separate from the clot before it is siphoned off into bottles. For the purpose of sterilization these bottles are fitted with rubber stoppers and caps and placed in a water-bath and heated to 60 C. for one hour on three successive days. While this temperature does not interfere with the protective power of the fluid, it is capable of destroying any germs which may have gained access while being collected. Such serum obtained from horses brought up to the maximum degree of immunity is that which should be employed in the treatment of persons bitten by venomous snakes.

As to the question of doses, there has been some difference of opinion, and while about  $2\frac{1}{2}$  drachms (10 c.c.) is the quantity that has been usually employed, D. Semple and G. Lamb<sup>1</sup> assume, from their experiments on rabbits, that a man of ordinary weight (about 60 kilos) bitten by a cobra may be saved by the injection of 4 drachms (15 c.c.) of Calmette's serum, provided the injection is made before the elapse of such time as is required for the absorption of a lethal dose of the venom. In severe cases 5, 8, or 10 drachms (20, 30, and 40 c.c.), or as much as 12 drachms (50 c.c.), should be employed to insure neutralization of the poison, especially so as no ill effects are capable of being produced by the serum. The antidote may be injected subcutaneously, or, better still, if rapid effects are desired, intravenously, and in addition a solution of calcium hypochlorite (1:160) should be injected into and around the bite. The antidote should be employed at the earliest moment possible after the wound has been inflicted; there are, however, numerous instances in which the serum has not been injected until the lapse of an hour and a half after the bite, and the patients recovered.

In connection with this subject it is interesting to note that Calmette does not consider that the antivenomous serum antidotes the action of the snake venom by forming with it a chemical combination, but that

<sup>1</sup> British Medical Journal, April 1, 1899.

its value depends upon a physiological process, in which the white blood-corpuscles are stimulated to carry on intercellular digestion, which he regards as a variety of phagocytosis.

**Apomorphine.** This derivative of morphine, which has been largely employed as an emetic, has recently been used as a nervous sedative. We are not inclined to believe that its sedative effects are in any degree due to contamination with the alkaloids of opium, as the doses in which it is found effective are so small that even the pure morphine would not be capable in these doses of exerting sedative effects. R. F. Lewis<sup>1</sup> secured satisfactory results in the treatment of delirium tremens with this drug. His original object in using the drug in such cases was for the purpose of evacuating the stomach, and he was at first surprised to note its marked sedative effect upon the patient, who before its use was intensely excited, but who became calmer immediately, and was controlled without difficulty after its use. Charles J. Douglas called attention to the marked hypnotic effect of apomorphine in October, 1899, and in a more recent paper<sup>2</sup> reiterates his former statement, that it is a most valuable hypnotic for the relief of insomnia, regardless of the cause. The usual dose employed is  $\frac{1}{80}$  grain (0.002 gramme), to be given hypodermatically after the patient has disrobed and placed himself in bed, as in some cases if the patient attempts to undress after receiving the drug vomiting ensues. In more susceptible persons  $\frac{1}{60}$  grain (0.0012 gramme) is less likely to produce emesis, while in others it is necessary to give larger doses to induce sleep. He finds that those who require large doses as a hypnotic appear also to be less liable to the emetic effect of the drug. If no hypnotic effect is obtained within half an hour the dose should be repeated, although usually it will induce sleep in ten to fifteen minutes. He asserts that the direct hypnotic effect lasts from one to two hours, but in many cases the sleep continues through the night, and the patient awakens the following morning without any disagreeable after-effects. A further advantage of apomorphine over many other hypnotics is that no drug habit is to be feared. In the insomnia resulting from withdrawal of morphine in persons accustomed to that drug he finds apomorphine acts with promptness and precision.

Dr. Philip Zenner<sup>3</sup> gives the history of a case of tachycardia in which apomorphine in large emetic doses gave relief in several attacks, but which after a time lost its effect and failed to exert any influence upon the severity of the attacks.

<sup>1</sup> New York Medical Journal, January 27, 1900.

<sup>2</sup> Ibid., March 17, 1900.

<sup>3</sup> Ibid., March 3, 1900.

**Arsenic.** On account of the slow elimination of arsenic, Dr. F. C. Railston<sup>1</sup> states that the administration of  $6\frac{3}{10}$  grains (0.42 gramme) of arsenous acid, or its equivalent, even if extended over a period of twenty-one days, is sufficient to produce peripheral neuritis in a child. He cites four cases in which symptoms of paralysis occurred in children after being treated for chorea with arsenic. In only one of the cases was there any of the ordinary mild toxic symptoms noted while the remedy was being administered, but the symptoms of neuritis developed gradually several days or a week after withdrawal of the arsenic. All of the cases ultimately recovered after a protracted convalescence.

While clinically testing dog and ox serum which contained arsenic, upon cases of pulmonary consumption, Dr. Lewis Kolutinski<sup>2</sup> observed that diarrhoea was checked in both the chronic and tuberculous varieties. As the serum was not stable and frequently gave rise to disagreeable effects, he was led to employ the hypodermatic injection of sodium arsenate, dissolved in normal salt solution, and obtained marked benefit in many cases of tuberculous enteritis. The quantity given at each injection is from  $\frac{1}{84}$  to  $\frac{1}{82}$  grain (0.001 to 0.002 gramme) of sodium arsenate dissolved in 60 minims (4 c.c.) of normal salt solution, given once a week in mild and convalescent cases and about twice a week in the average case, and every day when the diarrhoea was severe and the patient bed-ridden. Little or no pain is experienced from the injections, and in the majority of cases the patient speedily improved, so that the injections could be discontinued after thirty to sixty days. If the patient did not improve after being treated for fourteen days the injections were discontinued. It is not claimed that this method of treatment is a specific in all cases, but the results in the cases reported are undoubtedly most remarkable.

Trunecek<sup>3</sup> recommends as a radical cure for epithelial cancer the application of a solution of arsenous acid, 1:150, gradually increased to 1:80, in equal parts of alcohol and distilled water, to be painted over the affected area daily with a brush until the eschar forms. After repeated applications the eschar becomes black and is finally detached. As soon as this black crust is removed the applications are repeated, and if the crust produced is yellowish and is detached without hemorrhage no further treatment is required; but so long as it is black fresh applications should be made each time the crust is removed. The pain and inflammation are sometimes very severe, requiring subcutaneous injections of morphine, but the treatment, as a rule, should be interrupted only in exceptional cases. In ordinary cases of superficial cancer, as of

<sup>1</sup> Medical Chronicle, February, 1900.

<sup>2</sup> Medical News, August 11, 1900.

<sup>3</sup> Medical Record, New York, June 2, 1900.

the lip or face, from four to six weeks are required to effect a cure. The formula for Truncceek's first solution is as follows :

|                             |          |            |
|-----------------------------|----------|------------|
| R.—Acidi arsenosi . . . . . | gr. xv.  | gm. 1.00   |
| Aquæ destillatæ . . . . .   | f 3 ijs. | c.c. 75.00 |
| Alcohol . . . . .           | f 3 ijs. | c.c. 75.00 |
| Misce et ft. sol.           |          |            |
| Sig.—For local use.         |          |            |

The strength of the solutions in arsenic are gradually increased to 1 : 80.

|                             |         |            |
|-----------------------------|---------|------------|
| R.—Acidi arsenosi . . . . . | gr. xv. | gm. 1.00   |
| Aquæ destillatæ . . . . .   | f 3 x.  | c.c. 40.00 |
| Alcohol . . . . .           | f 3 x.  | c.c. 40.00 |
| Misce et ft. sol.           |         |            |
| Sig.—For local application. |         |            |

The following formula is credited to Ginestoux<sup>1</sup> for the destruction of cutaneous epitheliomata. It is said to be less painful than the arsenical pastes and solutions usually employed :

|                                  |        |             |
|----------------------------------|--------|-------------|
| R.—Orthoform . . . . .           | 3j.    | gm. 1.00    |
| Acidi arsenosi . . . . .         | 3j.    | gm. 1.00    |
| Alcohol . . . . .                | f 3 v. | c.c. 150.00 |
| Aquæ destillatæ . . . . .        | f 3 v. | c.c. 150.00 |
| Mix. Sig.—For local application. |        |             |

CACODYLATE OF SODIUM is an organic salt of arsenic, as will be noted from its formula :



It is a white, amorphous powder, soluble in water, tasteless and inodorous. It is said to become chemically active only after the breaking up of its molecule, and is, therefore, far less toxic than any other compound or preparation of arsenic. Ordinarily the dose is from 2 to 10 centigrammes ( $\frac{1}{5}$  to  $1\frac{1}{5}$  grains) ; but as much as 80 centigrammes (13 grains) have been given daily for several weeks without producing toxic effects. Ten centigrammes ( $1\frac{1}{5}$  grains) of sodium cacodylate are equivalent in arsenic to about 0.06 grammes (1 grain) of arsenous acid ; to 0.19 grammes (3 grains) of sodium arsenate, and to 6.15 grammes (100 minims) of Fowler's solution. Its therapeutic application is the same as that of the inorganic compounds of arsenic, except that it cannot be employed as a local irritant or caustic. The compound is best administered by hypodermatic or rectal injection, given daily for about ten days, followed by a rest of ten days. Loss of appetite and elevation of temperature are indications for temporary cessation of treatment.

<sup>1</sup> Philadelphia Medical Journal, September 8, 1900, p. 452.

Administered by the mouth it seems to be attended by disagreeable eructations, a garlic-like taste, pains in the bowels, diarrhoea, and general discomfort; but when given hypodermatically these disagreeable effects are not experienced. The following formula for hypodermatic use is given by Gautier:

|                     |           |          |      |       |
|---------------------|-----------|----------|------|-------|
| R.—Sodii cacodylat. | . . . . . | gr. c.   | gm.  | 6.40  |
| Aquæ destillat.     | . . . . . | f ℥ iij. | c.c. | 90.00 |
| Acidi carbolici     | . . . . . | ℥j.      | c.c. | 0 06  |

Boil, filter through sterilized filter and bring up to 100 c.c. (3 ounces) with distilled water. Each c.c. (16 minims) contains 5 centigrammes ( $\frac{5}{8}$  grain) of the salt.

H. Jambert and E. Badel<sup>1</sup> observed that after the injection of sodium cacodylate, arsenic can be found in the urine at the time of the first urination, and that its elimination continues for about a month. They verified the observations of A. Gautier, that cacodylate of sodium administered per os notably diminished the quantity of urine for several days.

Weidal and Prosper Merklen<sup>2</sup> experimented upon different patients suffering with tuberculosis and leucocythæmia with the cacodylate. Hypodermatic injections were made daily with doses of 0.05 and 0.10 gramme ( $\frac{5}{8}$  and  $1\frac{1}{2}$  grains), and in exceptional cases 0.02 gramme. In average cases of tuberculosis with advanced caseated pneumonia the treatment had little effect; but in the early stages, in which the lesion was still localized, cacodylate improved the appetite and strength and proved an excellent adjuvant to other measures employed against the disease. In two cases of pseudoleucocythæmia—a woman with adenitis and a man with lymphadenoma of the neck—the drug for some time stimulated the appetite and energy of the patient, but had little effect upon the blood or the evolution of the disease. In these doses cacodylate does not generally increase the number of white corpuscles, but the red corpuscles were rapidly increased in anæmic individuals. They were not, however, increased to the normal amount, nor after reaching a certain point could they be further increased, even by prolonged treatment. The increase in the number of red corpuscles in some cases persisted for a certain length of time, but after stopping medication in nearly all instances, after some days the number again fell to the percentage shown when the treatment was begun. The hæmoglobin was sometimes increased, but not in proportion to the red corpuscles.

Gerand<sup>3</sup> employed cacodylate by rectal injection for the treatment of chorea in three girls, aged eight, twelve, and fourteen years, with good results. They received during a period of fifteen days rectal injections of 5 c.c. (75 minims) of a solution of 0.25 per cent. The treatment

<sup>1</sup> *Semaine Médicale*, March 7, 1900.

<sup>2</sup> *Ibid.*

<sup>3</sup> *Ibid.*



was carried out as follows: For the first five days the injections were given daily; after a rest of five days two injections were given during the next five days, and three injections the following five days. The drug was well borne, and recovery took place in all cases.

A. Gautier insists upon the necessity of administering the drug hypodermatically. When given by rectum or per os he believes that the drug undergoes transformations which render it extremely toxic and dangerous. J. Grasset<sup>1</sup> does not agree with Gautier, and states that in the last sixteen patients to whom he has administered the remedy by the mouth none presented a garlicky odor upon the breath nor gastro-intestinal phenomena, but that in each of the patients the appetite was increased and they gained in weight.

**Aspirin.** Acetyl salicylic acid, under the trade name of aspirin, has been offered as another substitute for salicylic acid. It occurs in white, crystalline needles, sparingly soluble in water. It decomposes in the presence of alkalis, and when given internally passes through the stomach unchanged, but decomposes in the intestinal tract, from which it is absorbed. The daily dose for adults is from 40 to 80 grains. It is said to be well borne by the stomach when all other salicylates are rejected, and additional claims are made that symptoms of cinchonism are rare. It is difficult to conceive that any preparation containing salicylic acid, except in very small quantities, if absorbed would fail to produce this symptom, and if it is not produced after this preparation is given in full amounts we would be inclined to believe that it contains salicylates in too small a quantity to be therapeutically active or that absorption had not taken place. Liesau<sup>2</sup> was satisfied with the therapeutic effect of the drug, but frequently observed tinnitus. The preparation has been employed in the treatment of acute and chronic rheumatism, pleurisy with effusion, and in neuralgia by E. Grawitz, Herman Liesau, K. Nanasse, Friedeberg, and Floeckinger, who hold that while possessing the full therapeutic value of other salicylates it is to be preferred, as it does not produce gastric disturbances or tinnitus aurium. The drug possesses, in common with other salicylates, distinct antipyretic effects, and has been employed by Louis Renon and Latron<sup>3</sup> in doses of from 15 to 45 grains (1 to 3 grammes) to reduce the temperature in hectic fever. Considerable sweating follows its administration in these cases, and, as is well known, colliquative sweats decidedly depress such patients; it is extremely doubtful whether its use is justified under such circumstances. Its dose is from 10 to 30

<sup>1</sup> *Semaine Médicale*, March 14, 1900.

<sup>2</sup> *Deutsch. med. Wochenschr.*, May 24, 1900.

<sup>3</sup> *La Presse Médicale*, June 30, 1900.

grains (0.6 to 2.0 grammes), and is best prescribed in powders, pills, capsule, or cachets :

R.—Aspirin . . . . . ʒiv. . . . gm. 15

Pone in cachetas No. xxiv.

Sig.—One cachet after each meal.

**Bromipin**, another bromide for which good effects are claimed as a nervine and sedative, is a yellowish, oily liquid, made by the action of bromine upon oil of sesame, and is said to contain 10 per cent. of bromine. The usual dose is from one to four teaspoonfuls daily, either in the form of an emulsion or in soft capsules. Many prefer to administer it by rectal injection. In epileptics it may be given in doses of half an ounce daily by the rectum, and after six or seven weeks increased to an ounce, at which the dose should remain for two weeks and then again reduced to half an ounce. In A. Kothe's cases treated with bromipin the patients were placed upon a strict diet and put to bed for several weeks before the treatment was begun. It is not certain whether the marked improvement which took place should be attributed to the modification in the diet, combined with rest, to the method, as stated above, of giving bromipin, or to its superiority over other bromides. J. W. Frieser<sup>1</sup> and F. Schulze are favorable to the use of the drug, from which they had never seen bromism, either when given in large doses or in small doses, or when continued for a long time.

**Bromides.** Toulouse,<sup>2</sup> in collaboration with Richet, found that when they decidedly decreased the amount of sodium chloride in the diet of epileptics the therapeutic effect of bromides was markedly increased. He states that of twenty confirmed idiopathic cases of epilepsy in which the amount of salt in the diet was reduced to about 2 grammes (30 grains) a day he could lessen the dose of bromides from 60 grains (4 grammes) down to 30 grains (2 grammes) a day and still obtain marked beneficial results. One patient, who was having attacks every five days, went one hundred and eighty-four days without a seizure. No patients recovered under this treatment, nor was it expected; but periods between the attacks were prolonged in all cases. Roux confirms the statement of Toulouse and Richet, and suggests that the best method of reducing the daily amount of salt in the food was to place the patient upon a milk diet.

Neil MacLeod,<sup>3</sup> by administering enormous doses of sodium bromide, produced in patients a comatose condition, which he was pleased to call "bromide sleep." He made use of this method of treatment for the

<sup>1</sup> *Klinische therap. Wochenschr.*, May 27, 1900.

<sup>2</sup> *Revue de Psychiatrie*, January, 1900.

<sup>3</sup> *British Medical Journal*, January 20, 1900.

cure of the opium and cocaine habit, for the relief of obstinate vomiting in neurasthenic subjects, and also in two cases of acute mania. The method, which appears to us to be nothing more nor less than poisoning from sodium bromide, is carried out about as follows :

Upon the first day of treatment 2 drachms (8 grammes) of sodium bromide are given in a half-tumblerful of water every two hours until 1 ounce (30 grammes) has been administered. The treatment is repeated in the same manner upon the second day unless the patient is profoundly impressed by the quantity previously given. Although the patient may be decidedly impressed by the action of the drug, the full effects are not secured until twenty-four hours after the administration of the last dose, and when once developed continue for several days. He considers it a safe rule to cease the administration of bromides for twenty-four hours when drowsiness is so profound that the patient cannot be aroused, or, when aroused, talks incoherently. In case the sleep continues to become deeper no more of the drug will be needed. After the exhibition of these large doses the patient falls into a deep sleep, from which he cannot be aroused, and which lasts for from five to nine days. He cannot stand, walk, sit, or speak, but will pass the urine and feces in the bed if left to himself, or if placed upon the commode and held there for a few minutes, every six hours, he may be made to empty his bladder and rectum. During the continuance of the action of the drug seven glasses of milk should be administered during each twenty-four hours. If the patient is not able to swallow milk he should be placed in a half-sitting position and the milk fed to him out of a spoon, the chin being elevated to close the mouth, forcing the patient to swallow. Warm predigested milk may be administered also by the rectum. The room should be kept at a suitable temperature and the patient warmly clad and covered to prevent cold. Following the deep sleep consciousness returns, and the subject gradually recovers the power of locomotion, speech, etc., until about the fourteenth day of recovery, or in all about twenty-one days from the beginning of the treatment his condition becomes normal. Dr. MacLeod has employed this treatment in nine cases, seven of which have been previously reported. Opium, cocaine, and chloral habitués who had been accustomed to taking these substances in large quantities over a period of years were cured by the bromide sleep without suffering the usual symptoms noted upon their withdrawal. When they returned to their normal condition after the sleep the craving for the old drug had been lost. In one case—a cocaine and opium fiend—death took place on the seventh day of the treatment, and was attributed to double pneumonia. By recourse to this treatment in three cases of acute mania he was able to transport one case a great distance without other restraint or the excitement

of travel. In another, upon the twenty-third day after treatment, "no departure from the normal mental state could be noted." In the third case the patient died upon the sixth day of treatment; death was attributed to septic poisoning, beginning in the mouth as the result of injury from false teeth which had not been removed. The death-rate of two out of nine patients appears to be very high, and few of us would be willing to put into practice a method which if not dangerous in every case at least produces effects which are most alarming. The treatment would certainly be particularly dangerous in debilitated subjects and in those with renal insufficiency.

**RUBIDIUM BROMIDE** is claimed by Laufena<sup>1</sup> to be less depressing than potassium or sodium bromide, and he employs the following formula in the treatment of epileptics:

|                              |                |      |       |
|------------------------------|----------------|------|-------|
| R.—Rubidii bromidi . . . . . | 3jss.          | gm.  | 6.00  |
| Syrup. limonis . . . . .     | f3iv.          | c.c. | 15.00 |
| Aquæ dest. . . . .           | q. s. ad f3ij. | c.c. | 90.00 |

Misce. Sig.—One to two teaspoonfuls in water three times a day.

Each teaspoonful contains about 24 centigrammes (4 grains) of the salt.

**Bromoform.** During the past year bromoform has been employed rather extensively in the treatment of whooping-cough. Its taste is less disagreeable than the saline bromides, but its insolubility in water makes it more difficult to combine in prescription with other drugs, and it is distinctly toxic even in small doses. Doses that may be considered safe for administration to children are about one drop (0.03 c.c.) for each year of age, given from three to five times a day, according to the severity of the case. It is best administered by dropping upon sugar, but may be prescribed in emulsion or in a hydro-alcoholic vehicle. Wilbur L. Scoville suggests the following formula by which it may be given in an emulsion with a minimum quantity of alcohol. Each teaspoonful represents about 2 minims of bromoform, and the quantity may be altered to suit the individual cases. The bottle should be thoroughly shaken each time before the dose is poured out:

|                               |                |      |       |
|-------------------------------|----------------|------|-------|
| R.—Bromoformi . . . . .       | f3ss.          | c.c. | 2.00  |
| Tinct. tolut. . . . .         | f3j.           | c.c. | 4.00  |
| Mucilaginis acaciæ . . . . .  | f3ij.          | c.c. | 8.00  |
| Syrupi . . . . .              | f3iv.          | c.c. | 16.00 |
| Aquæ menthæ viridis . . . . . | q. s. ad f3ij. | c.c. | 60.00 |

Misce ft. emulsum.

The specific gravity of bromoform is nearly three times as great as that of water, in which it is quite insoluble, and if given in emulsion the greatest possible precaution should be taken to shake the bottle well before pouring out each dose, as the bromoform may accumulate at the

<sup>1</sup> Journal de Méd. de Paris, March 25, 1900.

bottom of the phial and a toxic dose given when the contents of the bottle have been nearly exhausted. Dr. Gay suggests that the best method of securing solubility is to add a small quantity of chloroform, which renders the bromoform freely miscible with water. The following prescription contains one minim of bromoform and half a minim of chloroform in each dose :

|                         |        |            |
|-------------------------|--------|------------|
| R.—Bromoformi . . . . . | ℥xxiv. | c.c. 1.50  |
| Chloroformi . . . . .   | ℥xij.  | c.c. 0.75  |
| Rum . . . . .           | f℥ij.  | c.c. 90.00 |

Misce. Sig.—Shake. Teaspoonful in water twice or thrice daily.

Dr. C. E. Stokes<sup>1</sup> reports two cases of bromoform poisoning which are of interest not only on account of the symptoms of poisoning and its treatment, but also as an illustration of the danger that may attend the administration of bromoform in an emulsion. Two children, one four years of age and the other two years of age, were being treated for whooping-cough and were taking a prescription made up so that each teaspoonful, which was to be given three times a day, represented half a minim (0.03 c.c.) of bromoform and 1 drachm (4 c.c.) of mucilage of tragacanth. At 8 P.M. the children each received a teaspoonful of the emulsion, which were the last remaining doses in the bottle. At 11 P.M. they were awakened and found to be giddy and confused and staggering in their gait. The symptoms became exaggerated, and when he reached them at 12.30 A.M. he found them unconscious, the limbs flaccid, the eyes closed, pupils contracted, respiration feeble in the elder child and stertorous in the younger, the breath smelling strongly of bromoform. The younger child ceased to breathe after about ten minutes, and artificial respiration was resorted to, and in a few minutes more it was necessary to resort to artificial respiration in the case of the elder child. By the hypodermatic use of strychnine and brandy, artificial respiration, and thorough irrigation of the stomach with hot water, followed by coffee, some of which was allowed to remain in the stomach, they rallied and breathed spontaneously after about an hour, although the elder child remained drowsy and stupid for a number of hours.

Another case of poisoning is reported by Dr. T. Brown Darling,<sup>2</sup> which illustrates one of the dangers of giving highly toxic substances in a concentrated form. For a little girl of six years he prescribed a 2 drachm (8 c.c.) phial of bromoform, of which two drops were to be taken twice daily. The child secured possession of the bottle and swallowed 1½ drachms (6 c.c.) of its contents. Immediately afterward she developed symptoms of intoxication and was given an emetic of mustard and also of ipecac, which acted promptly. Upon his arrival,

<sup>1</sup> British Medical Journal, May 26, 1900.

<sup>2</sup> Ibid., June 2, 1900.

shortly afterward, he found the child unconscious, in a state of collapse; pulse slow at the wrist, but the heart beating feebly and irregularly, at the rate of about 120 a minute. The respirations, which were about 8 to the minute, were very shallow, and the breath smelt strongly of bromoform. The face and lips were livid, the pupils markedly contracted and did not react to light, and there were no conjunctival reflexes. With a No. 11 soft-rubber catheter, to which a funnel was attached, the stomach was thoroughly washed out with warm water and sodium bicarbonate for about an hour and a half, until there was no longer any smell of bromoform, and before removing the tube coffee and ammonium carbonate were introduced into the stomach, and the same remedies were also given by rectal injection, and sinapisms were applied over the heart. The pulse gradually became stronger and more regular, respiration improved, and consciousness began to return in about two hours and a half from the time treatment was first commenced. In about half an hour more, which was three hours from the commencement of treatment, the child was able to answer questions, and after about fifteen minutes more he was able to leave her in charge of the parents, although she remained drowsy and stupid for a number of hours.

**Calcium Eosolate** is a creosote derivative, and is said to contain about 25 per cent. of that substance. It is a gritty, grayish powder, with a slight pungent, acrid taste, and is soluble in about ten parts of cold water and very sparingly soluble in alcohol. Its dose is from 5 to 10 grains (0.33 to 0.60 gramme), and is best administered in capsules, or may be given dissolved in water. It is somewhat more irritant to mucous membranes than other preparations of creosote. In small doses it has a tendency to produce constipation, but in large doses gives rise to diarrhoea, with griping pains in the bowels. Aside from its use in the treatment of bronchial and pulmonary affections it has also been employed by Heinrich Stein<sup>1</sup> in the treatment of diabetes insipidus and diabetes mellitus. In his cases there was a reduction in the amount of sugar and a decrease in the quantity of urine, and the patients gained in weight. The following formulæ employed by him met the different conditions in the treatment of chronic ulcerative phthisis:

|                                |                  |             |
|--------------------------------|------------------|-------------|
| R.—Calcii eosolici . . . . .   | 3j̄.             | gm. 7.5     |
| Aquæ font. . . . .             | f̄ 3 xijss.      | c.c. 50.00  |
| Extr. hyoscyami fluidi . . . . | f̄ 3 ss.         | c.c. 2.00   |
| Syr. pruni virg. . . . .       | f̄ 3 ij.         | c.c. 60.00  |
| Glycerini . . . . .            | q. s. ad f̄ 3 v. | c.c. 150.00 |

Misce. Sig.—Teaspoonful every three hours.

<sup>1</sup> Journal of the American Medical Association, February 24, 1900.

|                           |           |            |
|---------------------------|-----------|------------|
| R.—Heroin . . . . .       | gr. ijss. | gm. 0.15   |
| Calcii eosolici . . . . . | ℥ ij.     | gm. 8.00   |
| Aquæ . . . . .            | f℥ xiv.   | c.c. 50.00 |
| Syr. tolutani . . . . .   | f℥ ij.    | c.c. 60.00 |
| Glycerini . . . . .       | f℥ ij.    | c.c. 60.00 |

Misce. Sig.—Teaspoonful every three hours.

|                                |          |          |
|--------------------------------|----------|----------|
| R.—Calcii eosolici . . . . .   | gr. v.   | gm. 0.30 |
| Sodii bicarb. . . . .          | gr. v.   | gm. 0.30 |
| Carbo. animalis purif. . . . . | gr. xij. | gm. 0.75 |

Misce ft. chart. No. xxx.

Sig.—One powder four times daily.

|                              |                  |            |
|------------------------------|------------------|------------|
| R.—Calcii eosolici . . . . . | gr. lxxv.        | gm. 5.00   |
| Aquæ . . . . .               | f℥ ix.           | c.c. 35.00 |
| Extr. lobeliæ fld. . . . .   | ℥ viij.          | c.c. 0.50  |
| Aquæ . . . . .               | q. s. ad f℥ iij. | c.c. 90.00 |

Misce. Sig.—Teaspoonful every three hours.

|                              |          |            |
|------------------------------|----------|------------|
| R.—Calcii eosolici . . . . . | ℥ ijss.  | gm. 10.00  |
| Aquæ . . . . .               | f℥ ijss. | c.c. 70.00 |
| Sodii benzoici . . . . .     | ℥ v.     | gm. 20.00  |
| Syr. tolutani . . . . .      | ℥ ijss.  | c.c. 75.00 |
| Aquæ camphoræ . . . . .      | f℥ ijss. | c.c. 75.00 |

Misce. Sig.—Teaspoonful every two hours.

**Carbolic Acid**, even in dilute solution, if applied for a number of hours to an extremity, is capable of producing gangrene. This has been emphasized by Francis B. Harrington,<sup>1</sup> who in his service of five years at the Massachusetts General Hospital has seen eighteen cases, in a large proportion of which amputation of the finger was necessary, as the result of gangrene produced by applying dilute solutions of carbolic acid used as an antiseptic. Including these cases, he has been able to find in the medical literature of various countries a total of 132 cases of gangrene from dilute solutions of carbolic acid. Usually the patient has come to the hospital with gangrene which followed the use of carbolic acid, which was employed without the advice of a physician in the treatment of a felon, a bruise, a cut, or some other minor injury. In some cases the treatment had been suggested by a physician. His cases show that an aqueous solution of carbolic acid (1:5) is capable of producing gangrene if applied to an extremity, such as the finger or toe, for a number of hours upon a moist cotton or gauze dressing or in poultices. The gangrene results not from compression, but from carbolic acid. He quotes Levai and others, who have seen gangrene, subsequently requiring amputation, following the application of 2 per cent. and 3 per cent. solutions, and Péraire, who has seen the loss of the third joint of a finger in a child, aged ten years, after twenty-four hours' exposure to a compress saturated with a 10 per cent. solution of carbolic

<sup>1</sup> American Journal of the Medical Sciences, July, 1900.

acid. Gangrene does not always ensue after such application, but Harrington believes it to be far more frequent than is generally known. Frankenburg believes that gangrene results from the action of carbolic acid directly upon the red and white corpuscles, producing stasis thrombosis, and thereby cutting off nutrition.

During the past year carbolic acid has been frequently employed in the treatment of tetanus, and heroic doses have been administered without the development of toxic symptoms. Guido Baccelli,<sup>1</sup> noting that the drug powerfully diminished the reflex of the central nervous system, was led to its employment in the treatment of tetanus, administering, subcutaneously into and around the seat of infection, doses of  $\frac{1}{2}$  to  $\frac{3}{4}$  grain (0.020 gramme) every two hours until 6 to 12 grains (0.36 to 0.75 gramme) were given daily. He prefers this treatment to that by antitoxin, to which he considers it superior in therapeutic effect and more convenient and practical of application. G. Pinna<sup>2</sup> gives the statistics of Ascoli, in which 1 death and 32 recoveries took place when the carbolic-acid method was employed; 11 deaths and 32 recoveries following the use of Tizzoni's serum, and 13 deaths and 20 recoveries in which Behring's serum was employed. He reports a case of traumatic tetanus cured by Bacelli's treatment.

D. Flavel Woods<sup>3</sup> reports a case of traumatic tetanus recovering under carbolic-acid treatment. The wound was freely opened, scraped, curetted and immersed in a weak solution of carbolic acid for half an hour. Ten minims (0.6 c.c.) of a 10 per cent. solution of carbolic acid were administered hypodermatically; fifteen minutes later 20 drops were injected, and in thirty minutes more 30 drops were injected. During every half-hour for the rest of the day 30 drops of the solution were administered with  $\frac{1}{2}$  grain (0.03 gramme) of *cannabis indica*. At night the *cannabis indica* was discontinued, but the carbolic-acid solution was occasionally given. If comparatively quiet the patient was not disturbed, but when the attacks were prolonged the doses were increased to 1 drachm of the solution hypodermatically. On the second day, the patient being considerably improved,  $\frac{1}{2}$  drachm (2 c.c.) of the solution was administered every two hours. The treatment was continued until the morning of the third day, when drachm (4 c.c.) doses of the solution, to which small quantities of glycerin were added, were administered by the mouth until the spasms ceased. After this the solution was given in drachm (4 c.c.) doses, gradually reduced to  $\frac{1}{2}$  drachm (2 c.c.), three times a day until rigidity disappeared. Not until the third day was the patient able to swallow, and it was necessary to

<sup>1</sup> *La Riforma Med.*, 1889, vol. iii., p. 315.

<sup>2</sup> *Il Policlinico*, 1899, No. 17, p. 427.

<sup>3</sup> *New York Medical Journal*, September 9, 1899.



administer nourishment by rectal enemata. After this time he was able to swallow and was much improved, but rigidity did not entirely disappear for three weeks.

H. L. Nietert and R. F. Amyx<sup>1</sup> and D. S. Hanson<sup>2</sup> have used carbolic-acid treatment in tetanus. Nietert and Amyx saw four cases in the St. Louis Hospital, three of whom died. In the first case nineteen injections of a 2 per cent. solution of carbolic acid was employed. One-thirtieth of a grain was given at first, later increased to  $\frac{1}{15}$  to  $\frac{1}{2}$ , 2 grains, and finally  $3\frac{1}{2}$  grains. In all 21 grains were given during forty-eight hours, but no symptoms of carbolic-acid poisoning appeared. The second patient was given about 12 grains (0.75 gramme) in eleven injections during thirty hours, but also died. The third received 8 grains (0.51 gramme) in nine injections during sixteen hours, and death resulted. In all the above cases the strength of the solution used was 2 per cent. The fourth case was treated with a 10 per cent. solution, and during eight days received ninety-three injections or a total of 267 grains (16.3 grammes). The patient was not poisoned with carbolic acid, although he received 99 grains (6.6 grammes) during the first twenty-four hours. These cases appear to show that to be of value in tetanus carbolic acid must be used heroically. In Hanson's case, that of a youth, aged fourteen years, in whom symptoms of tetanus developed ten days after a pistol wound, recovery took place after the wound was freely opened and a quantity of shot and wadding were removed and the patient treated by injections of carbolic acid. During the first nine days three injections of a syringe-ful of a 2 per cent. solution of carbolic acid were given three times a day. After this time the number of injections were reduced to two a day and continued for two weeks longer. The boy recovered, although the quantity of carbolic acid was much smaller than has usually been proven to be effective in such cases.

J. Mitford Atkinson<sup>3</sup> reports a case of bubonic plague successfully treated in a Government State Hospital at Hong Kong by large doses of carbolic acid. The patient was a Scotchman, aged thirty years, and the case was one of great severity. During three days over 200 grains (13 grammes) of carbolic acid were given internally, with the result of lowering the temperature, allaying the vomiting, and relieving the mental depression, and ultimate recovery of the patient.

W. E. Fisher<sup>4</sup> reports a case of anthrax successfully treated by hypodermatic injections of carbolic acid into and around the seat of infection. The first injection consisted of 1 drachm (4 c.c.) of a 10 per cent. solu-

<sup>1</sup> St. Louis Medical Record, December 30, 1899.

<sup>2</sup> Cleveland Medical Gazette, October, 1899.

<sup>3</sup> Lancet, December 9, 1899.

<sup>4</sup> Therapeutic Gazette, August 15, 1900.

tion of carbolic acid, most of which escaped upon withdrawing the needle. During the following day 1 drachm (4 c.c.) of pure carbolic acid was injected into, beneath, and around the eschar. From this time the patient steadily improved.

Since the announcement of Phelps that 96 per cent. alcohol will entirely neutralize the effects of a local application of strong carbolic acid, the latter substance has been employed as a local application in the treatment of erysipelas, cellulitis, felonous ulcers, carbuncles, and, in fact, all inflammatory conditions where streptococci are present. Prevost<sup>1</sup> makes use of the following method of aborting erysipelas: The diseased surface is thoroughly cleansed and pure carbolic acid applied by means of a pledget of cotton saturated with carbolic acid and held with a pair of forceps. When the skin begins to turn white and considerable smarting develops, alcohol is applied freely to neutralize and wash away all of the acid. The parts are then covered with absorbent cotton and bandaged. No constitutional remedies are employed.

The neutralizing effect of 96 per cent. alcohol upon carbolic acid was fully demonstrated by Powell, who applied 95 per cent. carbolic acid to his hands, and after permitting it to remain for a few seconds thoroughly washed off the acid with alcohol, without producing harmful or disagreeable effects. He also called attention to the value of alcohol as a physical as well as a physiological antidote to carbolic acid if administered soon after the ingestion of the acid.

A very unusual case of poisoning in an infant, seven days old, in whom death resulted from an accidental local application of a very small quantity of carbolic acid on the skin of the abdomen, was reported by R. Abrams.<sup>2</sup> The nurse was preparing a carbolic-acid douche for the mother, and accidentally touched the pure carbolic acid with her thumb and index finger. Immediately afterward, while undressing the baby, she touched its right groin with her moistened finger, and five minutes later convulsions developed, and death ensued ten hours later.

Quite recently a case has come under my notice showing the extreme susceptibility of infants to local applications of carbolic acid. For an infant whose hand had been accidentally scalded, upon the suggestion of a neighbor an application of a proprietary remedy was made. Within about an hour pronounced symptoms of carbolic-acid poisoning were manifested, and continued in spite of active treatment for a number of hours.

**Carbonic-acid Gas.** The use of carbonic-acid gas by rectal injection is by no means of recent origin, but the article of A. Rose<sup>3</sup> has

<sup>1</sup> Montreal Medical Journal, January, 1900.

<sup>2</sup> Pediatrics, March 15, 1900.

<sup>3</sup> New York Medical Journal, January 6, 1900.

revived interest in the subject. The chief disadvantage to this method of treatment has heretofore been the inconvenience in securing the gas in a convenient form for application. This difficulty may be overcome by obtaining the gas under pressure in steel capsules, according to the system of Sterné. In these capsules the gas is furnished in any quantity. The smallest capsule, which is about the size of a large pill, can be conveniently carried in the vest-pocket, and contains sufficient gas for one application. When it is desired to give an injection, one of the capsules is attached to a bulb, at the end of which is a nozzle. The pressure and flow are easily controlled by a stopcock which is attached to the tube. Rose is enthusiastic in his recommendation of carbon-dioxide gas by rectal injection for the treatment of dysentery. Used by the same method in whooping-cough many cases were markedly benefited, the cough frequently disappearing entirely in about ten days. In some cases of the disease it appeared to have no effect whatever, but he has never seen it produce ill effects.

**Castor Oil.** From a number of articles which have recently been published it appears that by the systematic administration of castor oil two or three times a week many cases of obstinate and severe neuralgia may be cured. Encouraged by the report of Ochsner, who employed castor oil in the treatment of neuralgia, Harold N. Moyer<sup>1</sup> was led to try this treatment in fifteen cases of neuralgia. Of this number seven were either lost sight of or continued the treatment for too brief a period of time to permit of any definite conclusions. All of the eight remaining cases, some of which were very severe and which resisted all other forms of medication, with one exception, were either cured or markedly benefited. He believes the best method of administering the oil is in daily doses of 1 to 2 ounces (15 to 30 c.c.) in a glass of effervescent ale. Moyer does not believe that the beneficial effects should be attributed to the elimination of toxins through purgation, as in most cases after three or four days the oil ceased to act as a cathartic.

N. O. D. Parks<sup>2</sup> reports a case of severe supra-orbital neuralgia, in which other methods of treatment had failed, which was relieved by castor oil administered two or three times a week. It did not produce purgation in this patient, and he does not attribute its beneficial effect to the elimination of toxins.

Alva W. Knotts<sup>3</sup> reports a case of severe supra-orbital neuralgia, with which the patient had suffered for a number of years, and in whom various forms of treatment had been resorted to, without relief. For two months he administered the following prescription :

<sup>1</sup> Journal of the American Medical Association, April 21, 1900.

<sup>2</sup> Ibid., August 25, 1900.

<sup>3</sup> Ibid., September 1, 1900.

|                            |       |             |
|----------------------------|-------|-------------|
| R.—Olei ricini . . . . .   | f℥ij. | c.c. 90.00  |
| Glycerini . . . . .        | f℥ij. | c.c. 90.00  |
| Tinct. opii camph. . . . . | f℥vj. | c.c. 180.00 |

Misce. Sig.—A teaspoonful at bedtime.

The patient received one dose of this mixture every night at bedtime for the past two months, since which time she had experienced but one attack, and that a very mild one. Chronic constipation, with which she formerly suffered, entirely disappeared, and her general condition was greatly improved.

W. S. Caldwell<sup>1</sup> states that the credit of having first discovered the value of castor oil in the treatment of neuralgia should be given to Professor Gussenbauer, of Vienna. In 1886, having a patient upon whom he intended to operate for the relief of neuralgia, he administered castor oil and cascara sagrada. The man was so much improved by this treatment that the operation was postponed and the cathartic continued, and the patient recovered without operation. They both believe that beneficial effects are to be attributed to the elimination of toxins from the alimentary tract. In Merck's report the following formula is given for a palatable mixture of castor oil :

|                           |          |             |
|---------------------------|----------|-------------|
| R.—Saccharin . . . . .    | gr. xij. | gm. 0.72    |
| Olei gaultheriæ . . . . . | ℥xx.     | c.c. 1.30   |
| Alcohol . . . . .         | ℥iv.     | c.c. 16.00  |
| Olei ricini . . . . .     | Oj.      | c.c. 500.00 |

**Chloretone.** Trichlor-tertiary-butyl-alcohol, or acetone chloroform, under the trade name of chloretone, has during the past year been employed rather extensively as a hypnotic, mild anæsthetic, and antiseptic. It is a white, crystalline substance, with a camphoraceous odor and taste, sparingly soluble in cold water (1:100), but freely soluble in boiling water, alcohol, chloroform, and ether. It may be administered to adults in doses of from 5 to 10 grains (0.30 to 0.60 gramme), or in some cases as much as 20 grains (1.30 grammes); for children, doses should be proportionately less, repeated, if necessary, at intervals of from two to six hours. It is best prescribed in the form of powders, capsules, or, if a liquid is desired, whiskey may be used as a solvent or vehicle. As an anæsthetic, for use upon mucous membranes, or as an antiseptic, a saturated aqueous solution should be used, or it may be reduced to fine powder and used as an antiseptic by dusting it upon the wound.

E. H. Houghton and T. B. Aldrich<sup>2</sup> state that when administered to animals all degrees of hypnosis to complete anæsthesia may be produced for periods of various duration, depending upon the amount of substance

<sup>1</sup> Journal of the American Medical Association, August 11, 1900.

<sup>2</sup> Ibid., 1899, vol. xxxiii., p. 777.

absorbed. After extremely large doses it produces sleep and insensibility, lasting for several days. The respiration and pulse, which are but little disturbed by full or even large medicinal doses, after a time become slower and weaker, until death supervenes when lethal doses have been administered. Given by the stomach, the substance quickly passes into the circulation and into the blood. No spectroscopical changes can be observed in the blood. The pulse-rate is slightly lessened, but the action of the heart remains good until the organism begins to suffer from a lack of oxygen. The blood-pressure is usually unaffected by medicinal doses. The dominant action of the drug is confined to the central nervous system, and is essentially the same as that of the other anæsthetics and hypnotics of the fatty acid series, differing from them only in that it does not depress the circulatory system.

R. Rudolf<sup>1</sup> states that from his experiments upon animals little or no effect is produced upon the pulse, blood-pressure, or respiration when moderate doses are administered; but eventually if large enough doses are given the animal dies, the heart stopping first. On account of its tendency to lower bodily temperature and its slow elimination he advises that the drug should be used cautiously.

The safety of the drug as a hypnotic is apparently proven, even when taken in enormous doses, as was the case in a patient observed by William W. Donald.<sup>2</sup> A young man under Donald's treatment for the cure of the opium habit secured a quantity of chloretone, and during twelve hours took 120 grains (8 grammes). During the first four days after taking the drug he slept profoundly, but could be aroused with difficulty and made to drink water and evacuate his bladder and bowels. Upon the fourth day he was walked about the room by an attendant, and began to show signs of improvement. Upon the fifth day he could talk with difficulty, and upon this day he took light nourishment and dressed himself, and immediately lay down upon the bed and again slept profoundly almost the whole day. Upon the sixth day he dressed himself, ate breakfast, but was drowsy the whole day. He was restless upon the night of the sixth day, and began again to crave sedatives. The following day he was fully conscious. Sleep was continuous during the whole of the six days except when he was aroused to be given food or compelled to use the commode. In this case there were no alarming symptoms, and the only untoward effect noted was vomiting, which occurred upon the night of the second day after taking the drug. The pulse ranged from 85 to 104; respirations appeared to be somewhat deeper, but normal in number and rhythm; temperature toward

<sup>1</sup> Canadian Practitioner and Review, June, 1900.

<sup>2</sup> Therapeutic Gazette, January 15, 1900.

the close of the sleep became slightly subnormal as the result of exhaustion.

Freeman F. Ward<sup>1</sup> found chloretone to be a good hypnotic without disagreeable after-effects, and, in addition, of value to relieve the pain in gastric hyperacidity and to alleviate the severity and frequency of paroxysms in whooping-cough.

H. McI. Morton<sup>2</sup> found the drug of value in ophthalmic practice where a mild anæsthetic and antiseptic were required without at the same time affecting the pupil or power of accommodation. It does not produce corneal congestion, as does cocaine.

R. W. Wilcox<sup>3</sup> considers it a safe, reliable, and convenient hypnotic, and to more closely approximate the ideal theoretical hypnotics for the sleep phenomena.

In a case of senile chorea in which it was given in doses of 6 grains (0.36 gramme) every four hours, and also in a severe case of whooping-cough, E. A. Lea<sup>4</sup> used chloretone with marked beneficial effect. He considers it our most valuable hypnotic, and states that the sleep is soothing and satisfactory, and that no ill effects are experienced upon awakening.

Warren B. Hill<sup>5</sup> considers the drug a good local anæsthetic for operations upon mucous membranes, such as the pharynx, nose, and urethra, and its value is enhanced by its antiseptic properties. In insomnia he found it to induce natural sleep without depressing effect upon the circulation or respiration, and devoid of irritating action upon the stomach, bowels, or kidneys.

The following formulæ may be found convenient for practical use :

R.—Chloretone . . . . . ʒj. gm. 4.00

Ft. chartulæ (or tabellæ compressæ) No. xii.

Sig.—One to two powders (tablets) at bedtime to produce sleep.

R.—Chloretone . . . . . ʒss. gm. 2.00

Elix. aromat. . . . . f ʒ iij. c.c. 90.00

Misce et ft. sol.

Sig.—Shake well. One to two tablespoonfuls at bedtime.

Each tablespoonful of the second prescription contains 5 grains (0.32 gramme) of chloretone; each teaspoonful contains 1½ grains (0.08 gramme), and in that dose is suitable for children.

**Cocaine.** The discovery that anæsthesia might be produced by sub-arachnoid injections of cocaine should be credited to Dr. Leonard Corning, who published his results in the *New York Medical Journal* of 1885

<sup>1</sup> *Medicine*, Detroit, August, 1900.

<sup>2</sup> *Ophthalmic Record*, Chicago, March, 1900.

<sup>3</sup> *Medical News*, April 14, 1900.

<sup>4</sup> *Denver Times*, July, 1900.

<sup>5</sup> *New York Medical Journal*, August 18, 1900.

to 1888, but never made use of the method for performing surgical operations. A. Bier, of Kiel,<sup>1</sup> used the method upon his assistant, Hildebrand, and in turn had himself anæsthetized by the subarachnoid injection. T. Tuffier,<sup>2</sup> before the Surgical Society of Paris, presented a woman upon whom he had successfully operated for the radical cure of inguinal hernia after subarachnoid injection of cocaine. He had experimented with it since November, 1899, and after performing a number of minor operations with subarachnoid injections, resorted to the method for many major operations. In the *Semaine Médicale* of May 16, 1900, he reported sixty-two cases in which the method had been successfully employed, and since that report has successfully operated upon 107 additional cases. Operations have been performed upon the lower extremities, the perineum, rectum, abdomen, external and internal female genital organs, stomach, intestines, gall-bladder, and kidneys, but up to this time no operations had been performed above the diaphragm. In all cases where the injection was made into the subarachnoidal space absolute analgesia was produced without early or late complications. He believes the method to be practical, and may be used with safety and success. For making the injection he uses a Pravaz syringe, which may be thoroughly sterilized, having a platinum needle 9 cm. long, with an external diameter of 1.1 mm. and an internal diameter of 0.8 mm. This needle must be strong and non-flexible, so that it will not break or bend if brought in contact with the vertebra, and must end with a short bevel instead of an oblique bevel. The solutions employed for injection are freshly made and thoroughly sterilized 2 per cent. solutions of cocaine. His method of sterilizing is to place the solution in a water-bath of 80° C. for fifteen minutes; then keep it at a temperature of 38° C. for three hours. It is again brought to a temperature of 80° C. and allowed to cool to 38° C. This is repeated five or six times in succession in every instance. The injections are made as follows: The patient is placed in a sitting posture, with both arms carried forward. The seat of the intended injection is thoroughly antisepticized. The iliac crests are located, and an imaginary line connecting these two crests passes through the fifth lumbar vertebra. By injecting beneath this line you penetrate the medullary canal. Having located with the left index finger this spinal process, the patient is instructed to bend forward, which causes a separation of 1.5 cm. ( $\frac{3}{4}$  inch) between the one on which you have your index finger and the subjacent vertebra. The patient should be told that you are going to insert a needle and that he may feel some pain, but that he must not move,

<sup>1</sup> Deutsch. Zeit. f. Chir., 1899, vol. li.

<sup>2</sup> Journal des Praticiens, December 23, 1899.

for should he move the needle may be deviated from its proper course. He inserts the needle to the right of the vertebral column, about 1 cm. ( $\frac{1}{2}$  inch) from the line of the spinous process. The needle passes through the skin, the subcutaneous cellular tissue, the lumbar aponeurosis, the muscles of the lumbar region, and penetrates into the lamellar space and finally into the spinal canal. As soon as the needle is inserted into the subarachnoid space a few drops of clear, yellowish, cerebro-spinal fluid escapes. The injection should never be made until the surgeon has seen the cerebro-spinal fluid escape through the needle. If blood escapes through the needle it may be fluid blood or blood mixed with cerebro-spinal fluid, and as the only assurance we have that the needle has penetrated the subarachnoid space is the escape through it of the clear, yellow cerebro-spinal fluid, it is best in all cases to withdraw the needle and make another puncture when blood exudes through the needle. Being satisfied that the point of the needle penetrates through the subarachnoid space, the syringe is attached and 1 c.c. (16 minims) of a 2 per cent. solution of cocaine is slowly injected during a space of time of one minute. If this quantity is exceeded, although no alarming symptoms have ever been observed, epigastric anxiety is more marked and vomiting is more frequent. Having completed the injection, the needle is quickly withdrawn and the puncture closed with sterilized collodion. Note the precise time at which the injection is accomplished. After the lapse of from about eight to ten minutes the patient complains of a tingling sensation and numbness of the feet, which later extends to the legs. The operation may be commenced at this time. The sensation of touch is not lost. From four to ten minutes after the injection analgesia is usually complete, and continues from one to one and a half hours. It usually extends to the thorax and occasionally to the axilla. The analgesia is not partial, but complete.

In none of the sixty-three cases reported has Tuffier ever seen a serious accident. Usually the patients complained of a feeling of epigastric coldness. In fifty of the sixty-three cases emesis occurred. Headache occurs more frequently than emesis, but in two-thirds of the cases it is a very slight headache, and disappears on the following day after the operation. In some cases, however, the headache is so severe as to produce insomnia, and persists for forty-eight hours. Profuse sweating and dilatation of the pupil and some shaking of the limbs have been noticed, but all these symptoms disappeared within twenty-four hours after the operation. In fifteen cases elevation of temperature occurred on the day of the operation, but the following day the temperature was normal. In forty cases there was a chill after ten or fifteen minutes. Males and females, varying in age from twelve to sixty-nine years, have been successfully subjected to the puncture. He does not con-



sider it a suitable method of anæsthesia for children or hysterical individuals. If from any cause analgesia is not obtained the administration of a general anæsthetic, such as ether, should be employed. In his first experiments, before he had mastered the technique, it was necessary in several cases to etherize the patient after the injections of cocaine.

J. B. Murphy,<sup>1</sup> from whose paper I have freely quoted above, reports two cases in which subarachnoid injections of cocaine were successfully employed according to the method of Tuffier. The first was in a woman with pyosalpinx. She was entirely conscious throughout the operation, but did not experience the slightest pain. Nausea and vomiting occurred about six minutes after the operation began; her pulse at no time exceeded 75. After the operation the temperature reached 103° F. upon the same evening, after which it became normal, and no unpleasant symptoms occurred. In the second case the injection was made for the purpose of performing Schede's operation upon varicose veins of the leg. Thirteen minims of the solution were employed. Anæsthesia was complete in seven minutes. There was some nausea and vomiting during the operation; the pulse was not accelerated and was strong at all times, and the analgesia was complete. In another case the patient suffered from a sensitive ulcerated stump; eucaïne was substituted in the solution for cocaine. Some nausea and vomiting occurred. It was twelve minutes before analgesia was complete, and there was some return of sensation ten minutes after the operation was commenced. On the whole, it was not as satisfactory as cocaine.

Stimulated by the reports of Tuffier, S. Marx<sup>2</sup> undertook the study of the value of subarachnoid injection of cocaine in relieving the pain of labor, and presents a report of the histories of six cases in which the method has been employed with what appears to be a most remarkable result. He states that "it was very astonishing to see the parturient woman under the influence of cocaine lie quietly in bed, feeling only some indescribable sensation, but without pain; bearing down when told to, and giving birth to her child without her knowledge, and only cognizant of the fact when the first cry of the new-born was heard." Nausea, vomiting, headache, and elevation of temperature up to 103° F. on the evening of the day of delivery were experienced by some of the patients, but these passed off within twenty-four hours or were easily controlled by small doses of nitroglycerin, alone or combined with small doses of morphine. No severe complications were observed in any cases. Motor disturbances, so far as the uterus and its contraction

<sup>1</sup> Journal of the American Medical Association, September 1, 1900.

<sup>2</sup> Medical News, August 25, 1900.

are concerned, were not noted. In seven to twelve minutes after the injection the pain was very much diminished or entirely allayed, and the analgesia usually continued for about three hours, after which, if the labor had not been completed, the woman began gradually to feel the pain of uterine contractions. When analgesia was complete, only on command did the patient bring her abdominal muscles into play, and then as powerfully as if no cocaine had been used. The first case was that of a multipara, in whom, after the membranes had ruptured and dilatation was complete, a thoroughly sterilized solution of cocaine was injected, and the patient delivered herself spontaneously without the slightest pain, and the placenta came away after the lapse of ten minutes. The temperature rose to  $100.5^{\circ}$  F., but in a few hours returned to the normal without treatment. A slight throbbing headache was felt for some time, but disappeared without treatment in twenty-four hours. In the second case the injection was employed to produce manual dilatation, which was accomplished without pain. The head was brought above the brim of the pelvis, and the patient left unmolested to see if labor would proceed spontaneously. In twelve hours she broke out into a profuse sweat; temperature rose to  $102^{\circ}$  F., pulse 90, respiration 60; slight headache. Within twelve hours more her condition was normal, and upon the following day labor pains began and the child was born spontaneously. In the third case an injection was made without effect. In forty minutes another injection was made of the same solution. No effect having been produced and the patient having become hysterical, chloroform was administered and the woman delivered with forceps. Later on, the solution having been tested by various methods, it was found to be totally inert. In this case, which he considered to be an excellent control test, the fluid, which was a saline solution containing no cocaine, failed to produce anaesthesia. Within about three hours after the administration of the injection the patient complained of headache, tingling in the legs, slight nausea and vomiting, and in fourteen hours the temperature rose to  $102^{\circ}$  F., pulse 100, respiration 28. The condition returned to normal in eight hours. In the fourth case by the injection the patient was entirely relieved of pain and had no knowledge of uterine contractions, which occurred normally every two minutes. Forceps were applied and the child delivered without pain, although the patient was conscious that traction was being made. This patient had vomiting and slight headache, with a rise of temperature to  $101.5^{\circ}$  F., but returned to a normal condition within twelve hours. In the fifth case, after the subarachnoid injection, podalic version was performed without pain to the mother, although she experienced a feeling of suffocation when the hand was introduced into the uterus. During the version the uterus contracted

firmly around the operator's hand, so that manipulation was difficult. The sixth case was one of foot presentation, with rupture of the membranes. When the os was fully dilated the pains were not frequent, and the subarachnoid injection was administered. During the next half-hour the only change noted was slight dulling of sensation to pin prick and slightly delayed pain sensation. The injection was repeated, and the patient complained of burning in the lower extremities, with nausea, vomiting, and profuse sweating. Within thirty minutes more analgesia was complete; the hand was introduced into the uterus without pain, both feet brought down, and the child delivered without the knowledge of the mother. A second macerated child found in the uterus was delivered without pain. Considerable difficulty was experienced in delivering the placenta, and under chloroform anæsthesia it was still found to be impossible to remove it, as the uterus was in a spastic condition and the placenta adherent. The uterus was packed with gauze, and after about four hours, under cocaine narcosis, the hand was introduced into the uterus and the placenta pulled away. The uterine contractions were not as strong as normally and did not interfere with the manipulation. Within about an hour and a half nausea and vomiting developed, although anæsthesia continued. Three hours after the injection the temperature rose to 100.8° F., pulse 90, with some headache. Without medication the patient's condition returned to the normal within four hours. This patient had received half a grain of cocaine in less than seven hours. Until the method is further tried he does not recommend its introduction into general practice.

E. Blum and O. Kreis<sup>1</sup> employed with success subarachnoid injections of cocaine on six parturient women, of whom five were primiparas. In the first case, after dilation of the os was complete, subarachnoid injections of 1 cgm. ( $\frac{1}{8}$  grain) of hydrochlorate of cocaine were employed according to the method of Tuffier. After from five to ten minutes absolute analgesia of the lower portion of the body occurred and extended to the borders of the costal cartilage. The sensibility was lessened, but the voluntary movements were preserved. The uterine contractions continued with the same frequency and intensity as observed without the injections, and were painless. The normal pains produced by the pressure of the foetal head upon the soft portion of the pelvic floor disappeared soon after the injection. In two cases where expulsion occurred spontaneously there was no pain when the foetal head was expelled. In two cases it was necessary to apply the forceps, in one case the head coming last. No pain was experienced, and it was possible, without giving rise to the slightest pain, to suture

<sup>1</sup> *Semaine Médicale*, July 18, 1900.

the perineal and vaginal lacerations. No serious accident resulted from the use of the anæsthetic, and only two women suffered slight headache, with mild nausea and some vertigo. They found this method of anæsthesia equally as efficacious as in general surgery, but as yet the observations are too few from which to draw definite conclusions.

Doleris<sup>1</sup> reported to the Academy of Medicine of Paris his observations upon five parturient women in whom he had employed subarachnoid injections of 1 to 2 cgm. ( $\frac{1}{8}$  to  $\frac{1}{4}$  grain) of cocaine. Pains due to uterine contraction were removed in from five to ten minutes, and the analgesia thus obtained lasted from one to two hours. The contractions were more energetic, more frequent, and more prolonged after the anæsthetic. In the intervals the uterus remained in a state of semi-tension for a variable time. He does not consider it prudent to use cocaine in cases where podalic version may possibly become necessary. The loss of blood appeared to be less than usual. The effect of these injections had no apparent action upon the foetus.

Before the Section of Surgery at the International Medical Congress held at Paris, August 3, 1900, Severeanu reported the results obtained by him in which the anæsthetic had been employed many times in doses of from 1 to 4 cgm. He performed seventy abdominal operations under spinal anæsthesia, and although he had never observed a fatality, he does not believe it applicable to all cases. Alarming symptoms sometimes occurred and lasted for forty-eight hours, and in almost all cases where the method was employed nausea and vomiting followed.

R. Pitesci, in his observations upon 125 cases between the ages of five and seven years, in which medullary anæsthesia was performed, states that if the operation is practised for several times upon the same patient a tolerance to cocaine is acquired, and anæsthesia is not perfect. In the cases observed by him 17 out of 100 did not develop symptoms; 80 developed mild symptoms of intoxication lasting from twelve hours to five days, and 3 subjects showed symptoms of intoxication that endangered life. The dose employed was from 1 to 4 cgm.

Vincenzo Nicoletti, of Naples, believes that anæsthesia is due to circulatory disturbances, and to prove this he performed control experiments with ergot, antipyrine, and hydrochlorate of quinine, and produced anæsthesia somewhat similar to that produced with cocaine. He was unable to find any appreciable alteration of the nervous tissues.

**Creosote and Guaiacol.** These two substances so extensively employed in the treatment of bronchial and pulmonary affections, on account of their tendency to produce digestive disturbances, have to a certain degree been displaced by carbonic acid and other combinations

<sup>1</sup> *Semaine Médicale*, July 18, 1900.

which render them less disagreeable to the taste and also less liable to produce gastric derangement. Of the creosote derivatives, the carbonate, the valerianate, and the phosphate each enjoy certain advantages over the pure drug.

**CREOSOTE CARBONATE** (creosotal) is a thick, brownish, oily liquid, insoluble in water, with a slightly bitter taste, which in the intestines decomposes into creosote and carbonic acid. The initial dose of 5 drops, given three times a day, may be increased gradually to 30 drops at each dose without disturbing digestion. It is best prescribed in soft capsules, but if not distasteful to the patient may be administered in milk. In enormous doses of from 2 to 3 drachms, recommended by Chaumier, it upsets digestion and is disagreeable to take. The drug will be better borne if after being administered for a period of from six to eight weeks it is discontinued for a week; then begun again in small doses and gradually increased.

**CREOSOTE VALERIANATE** is an oily liquid, insoluble in water but soluble in alcohol. It is disagreeable in odor and taste, but it is less likely to produce digestive disturbances than creosote. Its dose is from 2 to 10 minims, and is best prescribed in soft capsules, in milk, or in the following mixture, suggested by Wainwright:

|                                  |         |             |
|----------------------------------|---------|-------------|
| R.—Creosoti valerianatis . . . . | f 3 v.  | c.c. 20.00  |
| Olei menthæ piperitæ . . . .     | gtt. x. | c.c. 0.60   |
| Alcohol . . . .                  | f 3 x.  | c.c. 300.00 |

Misce. Sig.—One to three drachms in milk, taken in three equal parts, daily.

Each teaspoonful of the above mixture is equivalent to about 12 minims of creosote valerianate.

**CREOSOTE PHOSPHATE** (phosphotal) is an oily liquid, smelling strongly of creosote; is soluble in alcohol but insoluble in water. It is best administered in capsules, in doses of from 2 to 10 minims.

**CRESOFORM** is an oily liquid, consisting of a combination of creosote and formaldehyde. It is employed locally as an antiseptic in the treatment of ulcers, anthrax, and to promote healing of tubercular lesions. In tubercular enteritis it may be given internally in doses of from 10 to 30 (0.60 to 2 grammes) drops three times a day:

|                       |         |            |
|-----------------------|---------|------------|
| R.—Cresoformi . . . . | f 3 iv. | c.c. 16.00 |
| Olei olivæ . . . .    | f 3 ij. | c.c. 8.00  |

Misce et pone in capsulas No. xxiv.

Sig.—One to three capsules three times a day.

**Guaiacol** and its preparations are employed with equal benefit in the same classes of cases in which creosote is applicable, and owing to its less irritating properties it is less likely to disturb digestion than creosote or its preparations. Moncorvo,<sup>1</sup> in commenting upon the difficulty in

<sup>1</sup> Bulletin de l'Académie de Médecine de Paris, September, 1899.

tropical countries of making an early differential diagnosis between intermittent malarial fever and tuberculosis, states that by locally applying guaiacol the true nature of the fever may be determined. When the fever is due to tubercular infection a prompt and decided fall of temperature occurs after such application, but in malarial fevers no such effect is produced. Whalen<sup>1</sup> successfully treated with guaiacol four patients affected with malaria after quinine and other remedies had been employed without curative effect. The beginning dose was 10 minims three times a day.

Christian<sup>2</sup> employed guaiacol locally in sixty-three cases of acute walking epididymitis. Fifty-six of the cases found relief from pain during the first twenty-four hours after the application, and among this number many were relieved in a few hours. The method pursued was as follows: The scrotum was gently massaged with a 20 per cent. ointment of guaiacol in lanolin, and the ointment was then spread upon lint and applied to the whole scrotum, which was then enveloped in a layer of absorbent cotton held in place by a suspensory bandage or a one-and-a-half-inch gauze bandage. The treatment was reapplied every second day until about the sixth day, when, after the inflammation had subsided, the following ointment was substituted for the one containing guaiacol:

|                      |           |       |          |
|----------------------|-----------|-------|----------|
| R.—Unguent. hydrarg. | . . . . . | 3 ij. | gm. 8.00 |
| Unguent. belladonnæ  | . . . . . | 3 ij. | gm. 8.00 |
| Ichthyol             | . . . . . | 3 ij. | gm. 8.00 |
| Lanolin              | . . . . . | 3 ij. | gm. 8.00 |
| Misce.               |           |       |          |

By this treatment many cures were effected in two or three weeks, and sometimes earlier. One of its greatest advantages is that the patient is not required to lie in bed.

The preparations of guaiacol which have attained the greatest popularity, and which are preferable to the pure drug for internal administration from the fact that they are still less likely to produce gastric irritability than the pure substance, are the carbonate (duotal), the valerianate (geosot), the sulpho-guaiacolate (thiocol), hydrochlorate-of-diethyl-glyocol-guaiacol (guaiasanol), and the phosphite of guaiacol.

GUAIACOL CARBONATE (DUOTAL) is a white, crystalline, non-irritating, odorless, and tasteless powder, said to contain about 90 per cent. of guaiacol. It is soluble in water and only sparingly soluble in alcohol. The dose for adults is from 2 to 20 grains (0.13 to 1.3 grammes), given three times a day, or in suitable cases up to 100 grains (6.6 grammes) daily. It passes through the stomach unchanged, but in the

<sup>1</sup> American Practitioner and News, Louisville, December 15, 1899.

<sup>2</sup> Therapeutic Gazette, March 15, 1900.

intestinal tract is split up into its component parts and is absorbed. This is probably the most valuable and largely employed salt of guaiacol, and appears to meet all the therapeutic indications for which the drug is given internally. It is best prescribed in powders or in capsules.

GUAIACOL VALERIANATE (GEOSOT), favorably spoken of by Wainwright in the treatment of pulmonary tuberculosis and gastric irritability, has been used to a limited extent. It is an oily liquid with a smoky odor, tastes first sweetish, becoming bitter. Its dose is 3 to 10 minims three times a day, and is best prescribed in soft capsules.

SULPHO-GUAIACOLATE OF POTASSIUM (THIACOL) is said to contain 60 per cent. of guaiacol. It is a fine, white, odorless powder, which is freely soluble in water. Its taste is first bitter and then sweetish. It is entirely non-irritating to the mucous membranes. The preparation is administered in doses of from 10 to 20 grains three times a day, but being non-toxic may be given in daily quantities of 225 grains. This is probably the most valuable soluble salt of guaiacol. Internally administered its value corresponds to that of guaiacol, for which it may be substituted, and may be given in very much larger doses than that drug without disturbing digestion.

DIETHYL-GLYCOCOL-GUAIACOL-HYDROCHLORATE (GUAIASANOL). Dr. Alfred Einhorn,<sup>1</sup> of Munich (with the assistance of Dr. Hütz), discovered a new preparation of guaiacol, which he calls guaiasanol, forming white crystalline prisms, is very soluble in water, having a slight odor of guaiacol, and has a salty, bitter taste. Its aqueous solution is neutral to litmus, and is precipitated by the addition of carbolyzed alcohol. In a 2 per cent. solution it is not irritating to wounds, but if used in greater concentration slight irritation is produced. Ten per cent. solutions give rise to decided irritation on sensitive mucous membranes. A 5 per cent. solution instilled into the eye at the beginning produces irritation, which is quickly followed by complete anæsthesia of short duration. In solutions of 1:50 and 1:100 it inhibits the growth of microbes, and may, therefore, be used as an antiseptic. Its antiseptic properties are about as great as those of boric acid. Hütz administered the drug to phthisical patients in daily doses of from 3 to 12 grammes in the form of powders by the mouth or by hypodermatic injection with concentrated aqueous solution. In the latter manner the drug is well absorbed, and injections of 3 to 4 grammes give rise to no local disturbance or untoward effects upon the blood, heart, kidneys, etc. Guaiasanol is, therefore, well borne when administered either by the mouth or by the hypodermatic method. The stomach was never

<sup>1</sup> Münch. med. Wochenschr., 1900, No. 1.

disturbed, and it was observed that the appetite was stimulated and that the patient took on weight. Furthermore, its good effects were noted by the improvement which took place in the tubercular lesion at the apices of the lung. By saturating the organism by the administration of large doses he was enabled to cure a case of tubercular meningitis. The remedy was also employed with satisfactory results in the treatment of tubercular diarrhoea. Favorable results were obtained in the treatment of ozæna by the local application of tampons soaked in a 10 to 20 per cent. solution of the salt and permitted to remain for one-half to one hour. After stopping the drug for several weeks the odor returned. The drug was also employed with benefit as a deodorant in gangrenous stomatitis, carcinoma, and sloughing ulcers. In the strength of 5:1000 to 1:1000 guaiasanol was employed by irrigation as a disinfectant in several cases of cystitis in which boric-acid irrigation could not be borne. Rapid improvement followed this treatment. In ophthalmic practice 1 per cent. solutions may be employed as an antiseptic in superficial injuries if slight anæsthetic effects are desired.

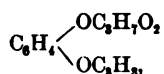
**GUAIACOL PHOSPHITE (GUAIOCOPHOSPHAL).** This is a white crystalline substance, soluble in alcohol but sparingly soluble in water. It has a pungent taste, but is non-irritating to the gastro-intestinal tract. It is said to contain over 90 per cent. of guaiacol. Its dose is from 5 to 10 grains three times a day, and is best prescribed in capsules or dissolved in wine or elixir. By some it has been used under the misconception that on account of being a phosphite the therapeutic effect of phosphorus as well as that of guaiacol would be obtained. This, however, cannot be the case, as neither phosphites nor phosphates possess in any degree the physiological action or therapeutic effect of phosphorus.

R.—Guaiacol phosphitis . . . . . ʒj. gm. 4.00

Ft. chart. No. xii.

Sig.—One powder dissolved in a little wine after meals.

**Guaiamar.** This substance, with the formula



is guaiacol-glyceryl-ester. It is formed by the action of anhydrous glycerin upon guaiacol, and is a white, crystalline powder, soluble in about twenty parts of water and freely soluble in alcohol. It has been employed as an intestinal and as a genito-urinary antiseptic. Usually it is decomposed only after reaching the intestinal canal, and is, therefore, less likely to produce gastric derangement than other preparations of guaiacol. In gastric dilatation with fermentation it is decomposed in



the stomach. George F. Butler<sup>1</sup> suggested its use in gastric dilatation with fermentation, as an antiseptic and genito-urinary antiseptic, and also in chronic bronchial and pulmonary affections. For the relief of painful joints in acute rheumatism he employed the following ointment :

|                       |              |     |       |
|-----------------------|--------------|-----|-------|
| R.—Guaiamar . . . . . | 3 ij.        | gm. | 8.00  |
| Lanolin . . . . .     | q. s. ad 3j. | gm. | 30.00 |

Misce. Sig.—Apply around the joint.

For gonorrhœal arthritis he employed the following formula :

|                               |       |     |       |
|-------------------------------|-------|-----|-------|
| R.—Guaiamar . . . . .         | 3 ij. | gm. | 8.00  |
| Unguent. belladonnæ . . . . . | 3 iv. | gm. | 16.00 |
| Unguent. hydrarg. . . . .     | 3 iv. | gm. | 16.00 |

For the treatment of bed-sores he suggested the following application :

|                                |              |     |       |
|--------------------------------|--------------|-----|-------|
| R.—Guaiamar . . . . .          | 3j.          | gm. | 4.00  |
| Balsam Peruv. . . . .          | 3j.          | gm. | 4.00  |
| Unguent. zinci oxidi . . . . . | q. s. ad 3j. | gm. | 30.00 |

The drug has been employed in the same cases of pulmonary affection in which guaiacol and creosote have been so largely used, and is said to be superior to these drugs by reason of the fact that digestion is not disturbed. The internal dose is from 2 to 10 grains three times a day. It is best given in capsules, or if desired may be given in mixtures or emulsions. Butler found it to be compatible with quinine, cod-liver oil, malt, and also with the hypophosphites.

**Crurin.** This new pharmaceutical product is rhodanate of bismuth and quinolin. It is a yellowish-white powder, insoluble in alcohol or water. K. Steiner<sup>2</sup> employed the drug successfully in the treatment of several cases of leg ulcer. After having reduced the œdema and inflammation by means of compresses soaked in a solution of aluminum acetate, he powdered the ulcer with crurin and covered it with a simple dressing. On account of pain, which results when the powder is first applied, it is better to mix it with equal parts of starch if the ulcer is extensive. Applications of crurin are made twice a day, and usually he succeeded in effecting cures in from two to six weeks.

**Digitalis.** The conflicting results obtained by different experimenters and clinicians as to the physiological action of digitalis and its principles is no doubt largely due to the varying amounts of the different glucosides contained in the leaves from which the preparations are made. Frequently the most beautiful specimens of the drug, from a botanical stand-point, are found to be inert. This is particularly true of cultivated digitalis, and is one of the strongest arguments in favor of the physiological standardization of preparations of this and a number of

<sup>1</sup> New York Medical Journal, 1899.

<sup>2</sup> Therap. Monatschrift, January, 1900.

other drugs. The conflicting opinions as to the physiological action of the different glucosides will probably not be reconciled until the different manufacturing chemists agree at least upon the physical appearance of these different active principles. At the present time there are several digitalins upon the market, some of which are soluble in water and some in alcohol, all having distinctly different appearances as well as chemical formulæ and physiological actions. Arnold and Horatio C. Wood, Jr.,<sup>1</sup> in experiments upon dogs with digitalin and digitoxin of Merck & Co., and with the *United States Pharmacopœia* tincture, found all of these to have identically the same physiological action upon the circulation. In medicinal doses the pulse was always lessened in frequency and the arterial tension increased, whereas in lethal doses the pulse was increased in frequency and became irregular, blood-pressure was lowered, and the heart stopped in diastole. The decrease in the heart's frequency was proven, to their satisfaction, to be due to the stimulation of the cardio-inhibitory mechanism, limited chiefly to the peripheral part of this apparatus. The rise in blood-pressure they considered to be due in part to an increase in cardiac power, but to a greater extent to constriction in blood paths. They agree with Bates that the dose in which digitalin is usually employed ( $\frac{1}{80}$  to  $\frac{1}{40}$  gr.) is too small, and advise it to be given in doses of  $\frac{1}{2}$  gr. Digitoxin apparently had the same physiological action upon the circulation as digitalis and digitalin, but, on account of its slow absorption and slow, irregular elimination, it is more likely to give rise to cumulative effects than the preparations just named. Furthermore, on account of its irritant action if given internally or hypodermatically, it is not recommended by them for human medication.

E. Zeltner<sup>2</sup> made a clinical study of Merck's crystalline digitoxin, and found that in doses of  $\frac{1}{4}$  milligramme ( $\frac{1}{320}$  of a grain) it was equal in promptness, energy, and duration to the preparations obtained from digitalis leaves.

The treatment of acute alcoholic delirium by enormous doses of digitalis, originally introduced by Fothergill and Jones, of England, has never been generally practised by the profession in this country, owing to the fear of poisoning the patients by the use of such a powerful remedy. That these facts are well founded may be seen from an analysis of the paper of Henry P. Loomis,<sup>3</sup> who employed the treatment in a series of ten cases. His cases were selected so as to include different classes of individuals—the strong, the weak, the young, the old, and those with nephritis and those with surgical complications. The

<sup>1</sup> American Journal of the Medical Sciences, August, 1900.

<sup>2</sup> Münch. med. Wochenschr., June 28, 1900.

<sup>3</sup> Medical News, August 18, 1900.

routine treatment employed was to administer  $\frac{1}{2}$  ounce (15 grammes) of tincture of digitalis every four hours until three doses were given. If the patient became quiet after the first, second, or third dose the remedy was discontinued. Another series of as many as three doses were given at intervals of six hours if delirium continued. The guide to the repetition of the drug was its narcotic effect. In this series of cases there were two deaths, five were benefited, and in three the drug promptly quieted the delirium, and the patients recovered more quickly than when under other methods of treatment. His conclusions were that the use of large doses of digitalis in acute alcoholism is fraught with danger; that the best results are to be obtained in young, strong, and robust patients free from complication; that unless narcosis occurs after three doses have been given the remedy should be discontinued.

**Diphtheria Antitoxin.** A review of the literature in reference to the employment of diphtheria antitoxin in the treatment of diphtheria cannot but convince us of the almost unanimous opinion of the profession as to its great value. Dr. E. Rosenthal<sup>1</sup> made a collective investigation as to the opinions of the physicians of this and other countries as to its therapeutic value in the treatment of diphtheria and also as an immunizing agent for those exposed to the disease, and he received replies in almost every instance which were favorable to its use, both as to its marked curative and prophylactic properties. As was to be expected, there were a few who expressed the opinion that their results had not been more satisfactory than by the methods formerly employed, and attributed the lower death-rate of diphtheria to the mildness of the epidemics of recent years rather than to the use of the antitoxin. As to the dose of the serum, while there is a tendency to give it in greater quantities than was done a few years ago, the general opinion is that this is to be regulated according to the severity of the infection and also by the period at which the case is first seen. In mild cases, if seen upon the first day, from 1000 units to 1500 units as an initial dose will usually suffice; but in the nasal and severe laryngeal, and all other cases in which there is severe infection, these doses should be markedly exceeded. In some cases as much as 8000 units are given at a single dose. In severe cases, however, it is considered, as a rule, better to employ a dose of about 4000 units, to be repeated in twelve hours, rather than the large dose as stated above. The death-rates have been greatly reduced since the more general use of diphtheria antitoxin, and there can be no doubt but that even better results would be obtained if the serum were more generally employed as an immunizing agent. The

<sup>1</sup> Journal of the American Medical Association, August 4, 1900.

doses for this purpose should be, irrespective of the age, about 750 to 1000 units. The more general employment of antitoxin has reduced decidedly the number of cases requiring intubation, and if used twelve hours or more prior to the operation the death-rate is lowered in such cases 50 per cent.<sup>1</sup> Dr. William H. Park, of New York,<sup>2</sup> makes a plea for the more general use of antitoxin as a prophylactic and gives the record of 6506 cases exposed to infection in which the serum had been employed as a prophylactic. Out of this number twenty-eight developed evidences of diphtheria within twenty-four hours, all of whom recovered. Twenty-seven developed diphtheria within thirty days, and all recovered. There was one, however, of this number who developed scarlet fever and diphtheria who died on the second day of the illness. In none of these cases were there harmful effects resulting from the inoculation. About 3 per cent. exhibited rashes and five-tenths of 1 per cent. more or less febrile disturbances. Many statistics could be quoted as to the value of the serum, but inasmuch as there can be no question as to its curative and prophylactic value no good purpose could be served by quoting them. There is probably no single therapeutic agent about which there is so little difference of opinion.

**Dormiol** is a yellowish, oily liquid having a camphoraceous odor. It is made by chemically combining amylene-hydrate and chloral. In doses of from  $7\frac{1}{2}$  to 15 grains (0.50 to 1 gramme) it has been employed as a satisfactory hypnotic by E. Schultze<sup>3</sup> and Peters.<sup>4</sup> On account of its disagreeable taste and peculiar properties toward water it is best administered in soft capsules. When equal parts of water and dormiol are mixed they do not combine at once, but separate into two distinct layers. If, however, they are shaken together and permitted to stand for two hours, and then shaken again, they are freely miscible and form a clear solution. By the further addition of water to this solution dormiol again separates. In acute mania Schultze failed to obtain satisfactory results from the use of dormiol. A convenient method of prescribing the substance is as follows :

R.—Dormiol . . . . . 3j.                      gm. 4.00  
 Pone in capsulas No. viii.  
 Sig.—One to two capsules at bedtime.

**Epicarin** is a derivative of beta-naphtol with creolin, for which it can be used as a substitute in the treatment of parasitic skin diseases and also in prurigo. Kaposi<sup>5</sup> prefers epicarin to creolin, believing it to be less irritating and less toxic. He gives the following formula,

<sup>1</sup> Journal of the American Medical Association, May 19, 1900, p. 1230.

<sup>2</sup> Ibid., April 14, 1900.

<sup>3</sup> Neurolog. Centralblatt, 1900, No. 6.

<sup>4</sup> Münch. med. Wochenschr., April 3, 1900.

<sup>5</sup> Ibid., 1900, No. 11.

which he considers valuable in the treatment of scabies, herpes tonsurans, and prurigo :

|                              |        |           |
|------------------------------|--------|-----------|
| R.—Epicarin . . . . .        | ℥ ijs. | gm. 10.00 |
| Unguenti . . . . .           | ℥ iij. | gm. 90.00 |
| Misce et ft. unguent.        |        |           |
| Sig.—Apply to affected area. |        |           |

If a liquid prescription is preferred the following may be employed :

|                          |         |            |
|--------------------------|---------|------------|
| R.—Epicarin . . . . .    | ℥ ijs.  | gm. 10.00  |
| Alcohol . . . . .        | f℥ iij. | c.c. 90.00 |
| Spt. lavendulæ . . . . . | f℥ vj.  | c.c. 25.00 |
| Glycerini . . . . .      | f℥ ijs. | c.c. 10.00 |

After epicarin has been applied for several days the skin becomes red and dry, with a tendency to cracking, and therefore in the treatment of pruritus after several days' use it is advisable to discontinue the applications of epicarin and apply diachylon ointment for a few days, after which the patient should take a warm bath before again applying epicarin salve.

**Erythrol Tetranitrate** is a white, crystalline substance, soluble in alcohol, insoluble in water, explosive on percussion. Its dose is from  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.015 to 0.03 gramme) three times a day, and is best administered in tablets. A convenient form of prescribing is as follows :

|                                      |           |          |
|--------------------------------------|-----------|----------|
| R.—Erythrol tetranitratiss . . . . . | gr. xij.  | gm. 0.77 |
| Sacchari lactis . . . . .            | gr. lxxv. | gm. 5.00 |
| Alcohol . . . . .                    | q. s.     |          |

Misce et ft. tabellæ No. xlviii.

Sig.—One to three tablets three times a day.

In the above prescription each tablet contains  $\frac{1}{4}$  grain of erythrol tetranitrate. When compounding the prescription forcible trituration should not be practised, as there is danger of producing an explosion.

B. Addy<sup>1</sup> relates a case of a patient with very severe angina pectoris, in whom other drugs had failed to bring relief, who was markedly benefited by the use of half-grain doses of erythrol tetranitrate. Sir William Broadbent<sup>2</sup> strongly recommended the drug for the purpose of relieving high arterial tension, and mentions a case of interstitial nephritis with high arterial tension and symptoms of uræmia in which the erythrol tetranitrate was used with the greatest benefit, and another case resembling Raynaud's disease which recovered by the use of the drug. Hugh Walsham<sup>3</sup> believes it to be a valuable vasodilator, and employed it in three cases of aortic regurgitation accompanied by cardiac pain. In three cases of chronic interstitial nephritis two were benefited.

<sup>1</sup> Medical Record, May 6, 1899.

<sup>2</sup> British Medical Journal, October 1, 1898.

<sup>3</sup> British Medical Journal, November 4, 1899.

**Eumenol.** Tang-Kui or Kau-Kui or Won-Wu (man-mo) or Schanki. Dr. Arthur Mueller<sup>1</sup> recommended the fluid extract of this plant as prepared by Merck, and placed upon the market under the name of eumenol, in the treatment of amenorrhœa and dysmenorrhœa. Heinz, who experimented upon animals, found it to be free from abortive influence and non-toxic, and Mueller confirmed these results by using the drug upon women at the beginning and near the end of pregnancy. Dose, 1 fluidrachm three times a day.

**Euphthalmin.** This synthetic alkaloid finds its greatest field of usefulness in ophthalmic practice where it is desired to produce a brief period of mydriasis without at the same time paralyzing accommodation or without fear of producing glaucoma. A. Darier,<sup>2</sup> for the purpose of comparison, instilled into one eye of a patient a 1 per cent. solution of homatropin and in the other eye a 5 per cent. solution of euphthalmin. He found that dilatation appeared somewhat sooner from homatropin than from euphthalmin, but after five to seven hours the mydriasis from euphthalmin ceased, but homatropin continued to act until the following day. A. B. Hill<sup>3</sup> found the drug valuable where dilatation of the pupil alone is desired. He observed that the drug did not affect accommodation or produce anæsthesia, had no effect upon ocular tension, and did not cause hyperæmia or ischæmia of the conjunctiva. It was without effect upon corneal epithelium, gave rise to no subjective symptoms, and was apparently non-poisonous when used in strength of 5 to 10 per cent. solutions. Dilatation of pupil comes on in about thirty minutes, and the mydriasis passes off in from five to seven hours. Gelanto Vinci<sup>4</sup> studied the physiological action of euphthalmin upon cold and warm-blooded animals, and noted a primary irritation of the nervous functions, manifested by restlessness, excitement, increased reflexes and respiration, followed by tonic and clonic spasms, opisthotonos, and irregular respiration, followed by general paralysis. Peripheral nerves, especially motor, were depressed. The heart was increased in frequency and showed the characteristic vagus paralysis as seen from atropine. Despite increased cardiac activity the blood-pressure falls as a result of paralysis of the vasomotor system. Salivation appears late in the case, and is due to an irritation of the secretory fibres of the chorda tympani. The dilatation of the pupil, which comes in from fifteen to thirty minutes after instilling two or three drops of a 2 per cent. solution into the eye, is due to paralysis of the nerves of the sphincter iris without irritation of the sympathetic dilator fibres.

<sup>1</sup> Münch. med. Wochenschr., June 30, 1899.

<sup>2</sup> La Clinique Ophtalmologique, January, 1900.

<sup>3</sup> Chicago Medical Record, February, 1900.

<sup>4</sup> Therapeutische Monatschrift, December, 1899.

**Fluorine.** The preparations of fluorine are so irritant to the gastric mucous membranes that they are rarely resorted to for internal administration. Max Heim has recently suggested an organic compound of fluorine, under the name of antitussin, for local application in whooping-cough. The formula for this substance as given by him is said to be difluor-diphenol 5 parts, vaseline 10 parts, lanolin 85 parts. His method of applying this preparation is to thoroughly wash the neck, chest, and interscapular region of the back, so as to soften the skin, and apply about two drachms of the ointment, and continue the rubbing until the salve is entirely absorbed.

**Formaldehyde** is a gas with a pungent odor, irritating to all mucous membranes and abrasions. It is soluble in water, forming a clear, stabile solution, which is highly poisonous if taken internally in concentrated form. It combines readily with hydrogen sulphide and volatile compounds derived from ammonia, and is therefore a powerful deodorant. Solutions of the gas precipitate albumin and produce rapid hardening of both living and dead tissues. The vapor is widely employed as a disinfectant, and solutions of the gas of various strengths are extensively used in general and special surgery. Being free from injurious effects upon furniture and other articles exposed to it, and also on account of its volatility, it seems peculiarly adapted for the disinfection of houses, ships, etc. While inferior to superheated steam or dry heat of high degree, it is probably one of our most reliable chemical disinfectants. Park and Guérard, from their observations, state that superficial disinfection of dwellings may be effected by generating the gas in not less than 1 per cent. by volume of strength in a tightly closed room for periods of two hours. The temperature of the room should not be below 52° F. By this means non-spore-bearing bacteria may be killed, but if anthrax bacilli or other spore-bearing bacilli are to be dealt with, at least 2 per cent. by volume of the gas should be generated, and exposure should continue for a long period. To satisfactorily disinfect bedding, carpets, and household articles of a similar kind, they should be placed in a specially constructed chamber and 10 per cent. by volume strength of the gas should be generated and the exposure continued at a temperature of 110° F. for three hours.

In from 1 to 5 per cent. aqueous solutions are employed for sterilizing catgut, catheters, and surgical instruments. In very dilute solution (1:1000 and 1:3000) it has been used with success in the treatment of gonorrhœa in both males and females. In the strength of  $\frac{1}{2}$  to 2 per cent., and in some cases much stronger, it is employed in the treatment of syphilitic, tubercular, and other foul ulcers. It frequently promotes rapid healing. In conjunctivitis, both simple and purulent, in otitis media, nasal catarrh, and ozæna a dilute solution of 1:2000 or 1:1000

has been resorted to with marked benefit. It should not be forgotten that even very dilute solutions sometimes give rise to intense pain when applied to mucous membranes or abraded surfaces, and therefore it is advisable in all instances to commence treatment with weaker solutions than those mentioned; if well borne, the strength of the solutions may be increased. Inhalations of air charged with small quantities of the gas have been found to be of value as an adjuvant to other methods of treatment in phthisis and in whooping-cough. Lardner Green<sup>1</sup> gives the following formula, which he considers the most satisfactory method of applying these inhalations:

|                       |          |             |
|-----------------------|----------|-------------|
| R.—Formalin . . . . . | f 3j.    | c.c. 4.00   |
| Glycerini . . . . .   | f 3jvss. | c.c. 18.00  |
| Aquæ . . . . .        | f 3v.    | c.c. 150.00 |

Misce. Sig.—To be used as an inhaler from four to six times during the twenty-four hours.

When the air-passages are unusually sensitive, ten drops of the aromatic spirit of ammonia may be added to the mixture, to prevent smarting.

In the treatment of hyperidrosis, bromidrosis, and for controlling severe sweats in phthisical subjects, formaldehyde is one of our most valuable agents. In sweating of the feet it is best employed by applying a 40 per cent. solution to the sole three times a day and between the toes once a day. Four or five drops should be applied within the shoe to disguise fœtor. When a solution of this strength cannot be tolerated, 30 per cent. or 20 per cent. solutions should be used. Hirschfeld<sup>2</sup> employed the drug with the most satisfactory results in controlling the sweating of phthisical patients. In these cases a mixture of equal parts of formaldehyde (40 per cent. solution) and absolute alcohol is applied to the anterior and posterior surfaces of the body with a short brush or cotton swab, care being taken to avoid contact of the solution with the nipple, genital organs, umbilicus and anus, or to any abrasions of the skin. If the lower extremities also are involved in the sweating an application may be made to them on the following day. When applying the solution to the surface of the body the clothing should be so arranged as to prevent the vapor set free by the warm body from being inhaled or from coming in contact with the eyes. Solutions of the strength stated above sometimes give rise to considerable burning pain in persons with sensitive skin and in children; therefore for such patients much more dilute solutions are recom-

<sup>1</sup> British Medical Journal, January 20, 1900.

<sup>2</sup> Berlin. klin. Wochenschr., 1899, No. 15, and Adler, Deutsch. med. Wochenschr.; Therap. Beilage, 1900, No. 10.



mended. Hirschfeld asserts that one application will sometimes control sweating for a week.

Martin F. Engelmann,<sup>1</sup> I. D. McFeely<sup>2</sup> and A. Ravogli<sup>3</sup> employed formaldehyde in the treatment of cutaneous cancers, warts, condylomata, and rodent ulcers. The ulcers should be thoroughly cleansed and in some cases cocainized before the application of formalin is made. McFeely treated a case of inoperable epithelioma of the larynx and neck by injecting solutions of formalin. On the first day five drops of a 25 per cent. solution of formalin were injected. The following day ten drops of the 30 per cent. solution; two days later fifteen drops of pure formalin in as much water were injected. His conclusions were as follows:

1. As much as half a drachm can be injected into the body without causing toxic symptoms.
2. Though powerful, it is less likely than other styptics to cause clotting.
3. Pure formalin is probably as safe as a dilution.
4. Undiluted it causes more rapid anæsthesia.
5. It retards cell multiplication and growth in malignant tumors.

He believes if any of the neoplasms owe their malignancy to low forms of organic life, formaldehyde, being destructive to these, is not only palliative, but cures may follow its wise use. Ravogli's method of treating cutaneous cancer with formalin is to cover the ulcer with cotton saturated with solution continuously applied for thirty minutes. The patient experiences rather severe pain in a few moments after the application, and mild dermatitis follows, but does not persist. After two or three days the carcinomatous nodules were changed into light yellowish masses which are adherent to the tissues and which gradually slough off, leaving healthy tissue underneath. The strength of the solution applied at the beginning was 4 per cent., gradually increased to 8 per cent. and 10 per cent., and finally pure formalin was used. In advanced cases of cutaneous cancers in which cures cannot be expected, compresses saturated with a 2 per cent. solution of formalin applied to the ulcer will cleanse them, remove the offensive odor, and diminish the seropurulent discharge. A. Ranelletti believes that one of the great advantages of formalin over other applications in the treatment of foul discharging ulcers is that, by its power of transforming sloughing tissues into an eschar, absorption of putrid products is prevented, thus minimizing septic infection.

<sup>1</sup> Medical Review, St. Louis, May 26, 1899.

<sup>2</sup> British Medical Journal, 1899, No. 2013, p. 273.

<sup>3</sup> Journal of the American Medical Association, November 18, 1899.

**Fortoin** is a yellowish, crystalline powder, derived by the action of formaldehyde upon cotoin. It is tasteless and has a cinnamon-like odor. Its dose for adults is about 0.25 gramme ( $3\frac{3}{4}$  grains) three times a day, but as much as 0.50 gramme ( $7\frac{1}{2}$  grains) has been administered without producing any ill effect. It may be considered as an astringent disinfectant and of value in the treatment of diarrhoea, particularly those forms dependent upon intestinal ulceration. Overlach<sup>1</sup> has employed the drug in the treatment of diarrhoea, and claims that its curative action is due to active dilatation of the bloodvessels, thereby increasing the nutrition to the mucous membrane. In eight cases of enteric fever in which he employed fortoin five were decidedly benefited. The following may be found a convenient method of prescribing the drug :

R.—Fortoin . . . . . 3j. gm. 4.00

Pone in capsulas No. xvi.

Sig.—One capsule three times a day.

The dose is to be followed by a glass of milk.

**Gelatin.** The subcutaneous injection of gelatin in the treatment of sacculated aneurisms and also for the control of hemorrhage has, during the past year, been extensively employed.

Fletcher,<sup>2</sup> in an article upon the treatment of aneurism by the method of Lancereaux,<sup>3</sup> states that in the nine cases under his observation none as yet could be reported cured, although one case of abdominal aneurism still under treatment had markedly improved, the tumor having decreased considerably in size. In the seven other cases there was an appreciable diminution in the subjective symptoms referable to the pressure of the aneurism. Contrary to the statement of Lancereaux that the injections did not give rise to pain and if carried out under strict antiseptic and anæsthetic precautions there should be no rise of temperature, in several of Fletcher's cases there was a distinct chill and elevation of the temperature to 103° F. following the injection, and the pain produced was in some cases intense and continued for five or six hours. It was clearly shown that the coagulability of the blood was increased, and although no cures had as yet been effected, he was convinced that there was some merit in the treatment, which should be further tried.

Geraldini<sup>4</sup> reports four cases of aneurism treated by rest in bed and subcutaneous injections of 2 per cent. gelatin solution. One case of aneurism of the innominate artery received forty-five injections, and

<sup>1</sup> Centralblatt f. innere Med., 1900, No. 9.

<sup>2</sup> Journal of the American Medical Association, January 27, 1900.

<sup>3</sup> PROGRESSIVE MEDICINE, September, 1899.

<sup>4</sup> Gazzetta degli Ospedali, February 4, 1900.

was entirely relieved from neuralgia and dyspnoea, with cessation of pulsation in the tumor and reduction in its size. Three other cases of aortic aneurism were greatly benefited, the tumors lessening in size and becoming firm. The pulsations became distinctly less and the subjective symptoms disappeared. There were no harmful effects or inconvenience further than a transient smarting resulting from the injections.

Lewis A. Connor,<sup>1</sup> in a paper read before the New York Academy of Medicine, reported three cases of aortic aneurism treated by gelatin injections. One case died as the result of rupture of the aneurism three days after the third injection, and in the two others the treatment was discontinued after the second injection on account of the severity of the pain. Dr. Lewis, at the same meeting, reported a very advanced case of sacculated aortic aneurism in which rupture occurred three days after the second injection. In neither of the above stated cases in which rupture occurred does it appear that the treatment was in any way responsible for the accident.

In February, 1900, A. Fraenkel<sup>2</sup> exhibited before the Berlin Society of Internal Medicine a pathological specimen removed from the aorta of a syphilitic subject who had been under treatment by gelatin injections for aneurism. The aneurismal sac was found to be filled with old clots which Fraenkel thought to be formed, without doubt, under the influence of gelatin injections.

Lancereaux and Paulesco,<sup>3</sup> before the Academy, detailed their clinical observations upon a number of cases of aneurism, many of which had been markedly benefited and some cured by gelatin injections. Lancereaux also presented an anatomical proof of the efficacy of subcutaneous injections of gelatin. The man from whom the specimen was removed had been presented to the Academy in June, 1897, and October, 1899. The patient died suddenly upon the night of December 4th, not from rupture of the aneurism, but probably from syncope, which is frequent in lesions of the aorta, and cannot be prevented by the gelatin treatment. No gelatin injections had been made for more than two months. Upon examination of the specimen, at about 3 cm. above the aortic valve anteriorly, could be seen a nearly circular opening, measuring  $3\frac{1}{2}$  cm. in diameter, through which the sac, which was the size of a child's head, communicated with the aorta. This sac was almost entirely filled with old and very firm clots, which excluded the blood and made rupture impossible.

While solutions of gelatin have undoubtedly proven of value in the treatment of hemorrhages and of sacculated aneurisms, they should be

<sup>1</sup> Medical News, August 11, 1900.

<sup>2</sup> Sem. Méd., March 7, 1900.

<sup>3</sup> Bulletin de l'Académie de Médecine de Paris, July 10, 1900.

employed with care in all cases in which there is congestion or inflammation of the kidneys, inasmuch as in such cases uræmic symptoms have followed the injections. As an instance of the fact that gelatin injections should be withheld in all cases in which the renal function is embarrassed, two cases of hemorrhagic nephritis are quoted by Max Freudweiler<sup>1</sup> in which ill effects followed the injections. In both cases the quantity of urine was decreased and the amount of albumin was almost doubled.

E. Karchery<sup>2</sup> tried upon five patients who had to undergo operation at the clinic of Professor Rydygier, of Lemberg, the gelatin injections, with the idea that these injections made before the operation would, perhaps, diminish the hemorrhage consecutive to the section of the tissues. Each patient received before narcosis a subcutaneous injection of 200 c.c. of 2 per cent. gelatin solution. During the operation he could observe the following effects :

The muscles seemed to be drier than in the normal state. The arteries and veins bled as usual, but the small vessels and capillaries bled but little, and the surface of the wound was rapidly covered with clots. That incontestable advantage of the gelatin injections was greatly destroyed by the complications which the patient showed. Thus in the patient who had undergone strumectomy, six hours after the operation such a severe hemorrhage took place that after the failure of the tight tamponment it was necessary to open the wound and to suture the rest of the capsule. In the second patient, where a lipoma had been removed, a large hæmatoma occurred which required not less than ten days for absorption. In two cases of extirpation of the breast, with curettement of the axilla, two coffeespoonfuls of liquid blood were found in the axilla after six days. Furthermore, at the level of the line of the suture there was a greenish discoloration, due to reabsorption of the hæmatin. Only in one case (extirpation of the goitre) was there no secondary hemorrhage. The prophylactic injections of gelatin have inconveniences which take their value away.

The strength of the gelatin solution usually employed for injections is about 2 per cent. in normal salt solution. Sometimes calcium chloride in small quantities is added to the solution, which in all cases must be thoroughly sterilized before being injected.

The following is the original formula employed to control hemorrhage by Paul Carnot :<sup>3</sup>

|                         |          |      |       |
|-------------------------|----------|------|-------|
| R.—Gelatin . . . . .    | 3 iijss. | gm.  | 50.00 |
| Calcii chlorid. . . . . | 3 ijsa.  | gm.  | 10.00 |
| Aquæ dest. . . . .      | Oij.     | c.c. | 90.00 |

<sup>1</sup> Centralbl. für innere Med., July 7, 1900.

<sup>2</sup> Klin. therap. Wochenschr., 1899, No. 37.

<sup>3</sup> La Presse Médicale, 1898, No. 94.

**Hedonal.** Methyl-propyl-carbonyl-urethane appears as white, acicular crystals freely soluble in alcohol and having a disagreeable taste. Its dose as a mild hypnotic is from one to two grammes (15 to 30 grains), and may be administered in whiskey or brandy, or, better still, in cachets. The drug has a slight tendency to lower blood-pressure as well as respiration, and during sleep the temperature is usually decreased about one degree. After its administration there is usually increased diuresis. Hedonal is a sedative to the central nervous system. It has been used with varying success by a number of writers as a hypnotic and nervous sedative. It is not sufficiently powerful to control maniacal excitement.

R.—Hedonal . . . . . 3j. gm. 4.00  
 Pone in cachetas No. vi.  
 Sig.—One or two cachets an hour before bedtime.

**Hetol.** Sodium cinnamate, or hetol, is a white, crystalline substance freely soluble in water. It has been recommended in the treatment of pulmonary tuberculosis, and may be given either by the mouth, subcutaneously, or by intravenous injections. The doses by the mouth are from  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 gramme) in pills or capsules three times a day. For intravenous injection the beginning dose is one milligramme ( $\frac{1}{84}$  grain), dissolved in water, to be given once daily and increased to sixteen milligrammes ( $\frac{1}{4}$  grain). Erwald has recently employed this method in the treatment of twenty-five cases of pulmonary tuberculosis, and has failed to obtain the beneficial effects claimed for it by Landerer.

R.—Sodii cinnamatis . . . . . gr. xlvij. gm. 3.00  
 Olei olive . . . . . fʒij. c.c. 8.00  
 Misce et pone in capsulas No. xxiv.  
 Sig.—One capsule three times a day.

**Holocain.** This synthetic product is exclusively employed in ophthalmic practice. The hydrochlorate is a white, crystalline powder having a slightly bitter taste, and dissolves to the extent of  $2\frac{1}{2}$  per cent. in water at ordinary temperature. It has recently been employed rather extensively in ophthalmic practice<sup>1</sup> as a rapidly acting anæsthetic and as a mild antiseptic. It has found its greatest field of usefulness in the treatment of corneal ulcers and as an anæsthetic for the removal of foreign bodies from the eye. The instillation of a few drops of a 1 per cent. solution produces anæsthesia which persists for from five to fifteen minutes. Unlike cocaine, it does not contract the bloodvessels

<sup>1</sup> PROGRESSIVE MEDICINE, 1899, Vol. II., p. 332.

nor dilate the pupil, nor does it affect intraocular tension nor paralyze accommodation.

|                       |        |      |      |
|-----------------------|--------|------|------|
| R.—Holocain . . . . . | gr. j. | gm.  | 0.06 |
| Aque dest. . . . .    | fʒ ij. | c.c. | 8.00 |

Misce. Sig.—For instillation into eye.

**Hot Air of High Degree.** There is much diversity of opinion concerning the value of hot air in the treatment of chronic rheumatism and gout, and, although it may have failed in promoting cures in many cases, there can be no doubt of its value in many other cases where it has been used in conjunction with massage and as an adjuvant to other forms of treatment. It is not a specific for chronic rheumatism, nor, upon the other hand, is it a useless agent, but employed wisely in suitable cases it is of undoubted value as an adjuvant in effecting cures in many obstinate cases. If employed recklessly or without due regard for the fact that it is capable of giving rise to serious injury, disappointment and discouragement will follow its use. The greatest precaution should be observed not to burn or scald the patient, and treatments should not be continued so long nor with such frequency as to exhaust the patient and bring about relaxation. In the most approved form of apparatus abundant means are provided for the escape of the vapor produced by sweating. The surface exposed to the heat should be well covered with some good absorbent material evenly and snugly applied. As persons with sensitive skins may be severely burned without having experienced pain during the application of the treatment, the heat should not be raised to a greater degree than 200° F. nor continued longer than twenty or thirty minutes when patients are subjected to the treatment for the first time. At a later period in suitable cases the temperature may be raised to 350° or sometimes to 375° F. and continued for the period of three-quarters of an hour to one hour. Those with degenerative changes of the bloodvessels and myocardium are not considered fit subjects for the treatment, as by the increase of arterial tension which comes on during the application of the heat an additional strain is put upon the bloodvessels and also upon the enfeebled heart. While considerable difference of opinion exists as to the value of dry heat in chronic rheumatism, gout, and arthritis deformans, all agree that hot air is one of our most valuable agents in the treatment of sprains, bruises, cellulitis, tendocellulitis, and any simple inflammation of joints, and individual observers have secured satisfactory results in the treatment of various forms of neuralgia, neuritis, myelitis, and phlebitis.

Louis A. Coffin<sup>1</sup> succeeded in curing two cases of obstinate joint

<sup>1</sup> New York Medical Journal, March 10, 1900.

rheumatism by applying the treatment with the Betz apparatus and the use of antiphlogistine, a substance called by him "Denver mud." F. G. D. Kerr,<sup>1</sup> applied the hot-air treatment in a case of acute gout, of which the patient was rapidly cured. He also uses the method in the treatment of chronic rheumatism, phlebitis, sciatica, sprains and stiffening of the joint. The Lansing apparatus was used, and he found that debilitated and anæmic and even delicate patients bore the treatment well. The best results were obtained by applying the heat to the whole body, although only one joint or limb was involved. Homer Gibney<sup>2</sup> describes a portable hot-air box with which he has successfully treated gonorrhœal arthritis, chronic joint rheumatism, tendocellulitis, sprains, and also a mild case of arthritis deformans of the hand. While the most satisfactory results were obtained in the cases reported, he states that he has seen many other cases of rheumatic arthritis in which the symptoms were equally as well marked, but which did not respond to the treatment so promptly, and concludes that superheated air does not always give decided results, but in some cases is indicated as an adjuvant. Harold N. Moyer<sup>3</sup> believes that the apparatus manufactured in this country for applying hot-air treatment does not carry out the principles embodied in the original Talamon-Sheffield apparatus, so largely employed in England. His chief objection to the forms of apparatus most commonly employed is that the chamber is too small and the arrangement for obtaining a free supply of air for the escape of moisture deficient. He describes an apparatus devised by himself, in which these objections are overcome. By the application of the hot-air treatment in conjunction with passive movements of the joint and massage of the whole limb he was able to obtain good results in most of his cases of joint trouble following rheumatism and traumatism, and in other cases of chronic synovitis with adhesion in the joint. The treatment was applied also in certain nervous affections, such as peripheral neuritis, sciatica, and secondary joint troubles which follow paralytic attacks. He states that the results in many of these cases have been brilliant, and records a number of cases that bear out his statements.

Rudolph Klapp<sup>4</sup> reports a number of cases of joint affections which were greatly benefited or cured by the application of the hot-air treatment. David Walsh<sup>5</sup> employed the treatment with benefit in sciatica, lumbago, writer's cramp, chorea, stiffened and painful joints, gonorrhœal arthritis, asthma, chronic bronchitis, rheumatism, and gout.

<sup>1</sup> Practitioner, October, 1899.

<sup>2</sup> Therapeutic Gazette, July 15, 1900.

<sup>3</sup> Münch. med. Wochenschr., June 5, 1900.

<sup>4</sup> Medical News, July 21, 1900.

<sup>5</sup> Lancet, August 18, 1900.

**Hydrogen Peroxide.** Solutions of hydrogen peroxide have sometimes been employed to control slight cutaneous hemorrhages, but R. Platon<sup>1</sup> goes further and makes use of the solution for controlling hemorrhage from the mouth, nose, and uterus. In uterine hemorrhage he employed it in two cases by injection directly into the cavity of the organ. In the first case there was profuse hemorrhage of an anteverted and infected uterus. There were also cellulitis and parametritis. As the patient refused to be curetted, he gave uterine injections of peroxide of hydrogen. On two occasions four cubic centimetres were injected after dilatation with a laminated tent. The vaginal injection was then given and the vagina packed with antiseptic gauze. Bleeding was controlled and the inflammatory condition improved, but the patient continued to suffer with dysmenorrhœa of a mild degree for some time.

In the second case, in which intra-uterine injections of peroxide of hydrogen were found to be of benefit, there was profuse hemorrhage occurring at irregular periods as the patient was nearing the menopause. We do not believe this to be a safe method of controlling uterine hemorrhage unless the organ is thoroughly dilated to permit the free escape of gas which is always generated when solutions of peroxide of hydrogen are brought in contact with unhealthy tissues.

Baroux<sup>2</sup> states that peroxide of hydrogen in the form of vapor will certainly control whooping-cough within a week. His method consists in moistening sheets or pieces of cloth about a yard square with 80 grammes of solution of hydrogen peroxide and suspending them upon strings stretched across the centre of the room, the moistening to be repeated every four hours. This is the quantity ordinarily employed in a close room of from 60 to 75 cubic metres. Two rooms should be used, one for the day and the other for the night. The strength of the solution of peroxide should not be less than twelve volumes. About two quarts of the solution should be employed during seven days.

**Ichthalbin.** Ichthyol albuminate (ichthalbin) is a grayish-brown, odorless and almost tasteless powder, said to represent about 75 per cent. of ichthyol. It is insoluble in water except upon the addition of alkalies, and has been employed internally in doses of from five to thirty grains (0.30 to 2 gm.) as a substitute for ichthyol.

It is best prescribed in the form of powders, capsules, cachets, pills, or, if a liquid prescription is desired, it may be administered in water to which some mild alkali has been added for the purpose of rendering it soluble. Samuel Wolf<sup>3</sup> has administered the drug internally in a variety of diseases, and states that in all conditions in which the mucous mem-

<sup>1</sup> *Annales de Gyn. et d'Obstet.*, January, 1900.

<sup>2</sup> *Gazette des Hôpitaux*, March 24, 1900.

<sup>3</sup> *Merck's Archives*, January, 1900.



branes are hyperæmic and secretion is increased or perverted it is of decided benefit. He also found it valuable as a dusting powder in such cases in which ichthyol has usually been employed. He states that ichthalbin is non-toxic and non-irritating to the stomach, and can be given in practically unlimited doses. It is an intestinal antiseptic, a tonic to the stomach, and an aid to constructive metabolism. It is easily administered, and is neither disagreeable in taste nor odor.

Rolly and Saam<sup>1</sup> employed the drug in eight cases of simple chronic enteritis, three cases of chronic enteritis with peritonitis, five cases of tubercular enteritis, and twelve cases of subacute catarrh of the stomach and intestines, and were well satisfied with the results obtained. Their conclusions are as follows :

1. Ichthalbin in doses of as much as 8 grammes (3ij) a day, given for a long period of time, is entirely without ill effects. Even in such doses it does not produce gastric or intestinal irritation or constipation.

2. By the administration of from 30 to 50 centigrammes (gr. v to gr. viiss), three times a day, the appetite was stimulated and the weight increased.

3. Its action upon the intestinal fermentation was positive, and it was found by the administration of daily doses of from 1.5 grammes (gr. xx) to 3 grammes (gr. xlv) the quantity of ethyl-sulphuric acid was permanently reduced in all four tests made. The doses recommended in chronic intestinal catarrh in children are as follows :

Under one year of age from 30 to 50 centigrammes (5 to 7½ grains) three times a day ; from one to five years of age, ½ to 1 gramme (gr. viij to gr. xv) three times a day ; and above five, 1 gramme (gr. xv) three times a day.

Used as a tonic, somewhat smaller doses should be given.

For diarrhoea the following formula may be found practical in subacute and chronic diarrhoea :

|                          |      |     |       |
|--------------------------|------|-----|-------|
| R.—Ichthalbin . . . . .  | 3ij. | gm. | 8.00  |
| Bismuthi subnit. . . . . | 3iv. | gm. | 16.00 |
| Pulv. aromat. . . . .    | 3ss. | gm. | 2.00  |

Misce et ft. chart. No. xii.

Sig.—One powder every two to four hours.

For a child of two to four years with subacute or chronic intestinal catarrh :

|                         |                 |      |       |
|-------------------------|-----------------|------|-------|
| R.—Saloli . . . . .     | gr. xxx.        | gm.  | 2.00  |
| Ichthalbin . . . . .    | 3ij.            | gm.  | 8.00  |
| Misturæ cretæ . . . . . | q. s. ad f 3ij. | c.c. | 60.00 |

Misce. Sig.—Shake. Teaspoonful every three or four hours.

<sup>1</sup> Münch. med. Wochenschr., April 3 and 24, 1900.

**The Mammary Gland.** Extract of mammary gland was first employed by John B. Shober<sup>1</sup> in the treatment of certain forms of uterine hemorrhage. In a later paper upon the subject<sup>2</sup> he calls attention to the unwise administration of the drug by physicians, who appear to be ignorant of its limitations, in the treatment of a variety of uterine diseases for which it is entirely unsuited. He employs the desiccated mammary gland of sheep in the form of tablets, each of which represents 20 grains (1.30 gm.) of the fresh gland, in doses of three to six tablets daily. The gland produces no unpleasant systemic effects, but appears to have a very positive action upon the uterus, causing contraction of the uterine muscle, thereby diminishing the blood-supply and thus controlling bleeding. He compares its action upon the uterus to that of ergot, to which it is far superior, being far more reliable and surer in action; an additional advantage is that it can be used for long periods of time without causing unpleasant symptoms. By the use of the gland, bleeding, as the result of uterine fibroma, may in many cases be brought under control in a few weeks, and if persisted in the menstrual flow becomes regular and normal and free from clots. The growth of tumors is inhibited and diminishes in size up to a certain point. The bleeding being brought under control, the general health improves and the patient is placed in a far more favorable condition for operation. In some cases the continuous use of the gland may possibly indefinitely postpone the necessity for the operation. He believes that if by the use of the gland the tumors cease to increase in size and no degenerative or inflammatory changes take place in the tumor or adnexa, and if the flow becomes normal, we are not justified in submitting the patient to a major operation. Should inflammatory or degenerative changes take place or serious pressure symptoms persist, operation should be resorted to. The gland has also been employed in subinvolution of the uterus, providing there are no malignant or structural changes. In many cases leucorrhoeal discharges and bleeding cease, and backache and other reflex symptoms disappear. He plainly states that this was the only class of cases in which he has advised the use of the gland

R.—Tabellæ extracti mammæ . . . . . ʒʒ gr. v

No. c.

Sig.—One to two tablets three times a day.

Hermann J. Boldt<sup>3</sup> has watched a number of cases of myofibroma of the uterus in which thyroid and mammary extract were used, and states

<sup>1</sup> Philadelphia Medical Journal, November 11, 1899.

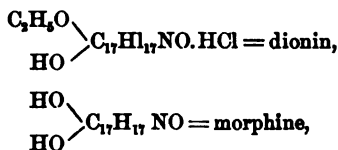
<sup>2</sup> Journal of the American Medical Association, July 28, 1900.

<sup>3</sup> Ibid., August 4, 1900.

that he has seen three cases of undoubted improvement in every respect, even a slight diminution in the size of the tumor. Upon the whole, he considers the value of these remedies at best rather uncertain.

**Morphine Derivatives.** Physicians have urged the manufacturing chemist to the further production of morphine derivatives which would be capable of relieving pain, inducing sleep, quieting irritations, and be free from the disagreeable after-effects of morphine, namely, nausea, vomiting, constipation, and a tendency to check secretions. The results of the combined efforts of the physician and chemist are offered to the profession at large in the two substances dionin and heroin, both of which have found favor with many physicians.

**DIONIN, OR ETHYL-MORPHINE HYDROCHLORATE.** Professor von Mering suggested to E. Merck a further investigation upon the derivatives of morphine, in order, if possible, to find a drug that, while sedative, antispasmodic, and analgesic, would be free from or possess to a less degree the disagreeable features of codeine or morphine. From a comparison of the formula of dionin with that of morphine—



it will be seen to be a substitution product from morphine in which the ethyl radical has replaced one hydroxyl group. The physiological action and therapeutic uses of dionin will be found to closely correspond in many respects with that of morphine. It is probably less depressing upon the respiration and less likely to disturb digestion. Dionin is a white, crystalline substance, readily soluble in water and also in alcoholic liquids. Its taste is less bitter than that of morphine or codeine. The dose is from  $\frac{1}{8}$  to  $\frac{1}{4}$  of a grain (0.01 to 0.02 gm.) three times a day.

H. Winternitz,<sup>1</sup> in a series of experiments, saw no cases in which respiration was decreased in frequency or volume under the dose of  $\frac{3}{4}$  to 1 grain (0.04 to 0.06 gm.) given either by the mouth or subcutaneously. In a second series of experiments there was an increase in respiratory volume during the first and second hour after the administration of dionin.

Paul Heim<sup>2</sup> employed the drug in bronchitis and pulmonary tuberculosis to relieve the cough and promote expectoration, and also to relieve pain in neuralgia, renal and hepatic colic, carcinoma, and in ulcer of the

<sup>1</sup> Therap. Monatsheft, September, 1899.

<sup>2</sup> Klin. Therap. Wochenschr., November 12, 1899.

stomach, peritoneal irritations, and pleurisy. In two cases—one of renal calculus and another of gastralgia—probably of nervous origin, it did not act well, but upon the whole the results were entirely satisfactory. He considers it more of a sedative than codeine, but less powerful than morphine. It does not check the bronchial secretions, nor is it so constipating as morphine. It quickly induces sleep in some cases, although some patients were made more wakeful under its influence. He does not agree with Herwick<sup>1</sup> that the drug does not produce euphoria, but asserts that this state was induced in many of his patients. It was rarely necessary to increase the frequency or the quantity of the dose, and no patient acquired the habit. Some patients, however, objected to the discontinuance of the drug. There were a few cases of nausea, vomiting, vertigo, and headache.

Janisch<sup>2</sup> used the drug with satisfactory results in the treatment of chronic bronchitis, pulmonary tuberculosis, and in asthma, and states that in these diseases it may be employed to supplant morphine. His results were less satisfactory in acute bronchitis. In his opinion it does not lessen irritability of the respiratory centre, but promotes expectoration. No disagreeable effects, such as nausea, vomiting, or constipation, were observed by him during the use of the drug.

Meltzner<sup>3</sup> used the drug with success in relieving cough in various diseases of the respiratory tract and also depression, irritabilities, and hallucinations of slight and mild degree in melancholia. The respiratory centre was not depressed or secretions checked, and expectoration was not interfered with. He agrees with Filhne that the drug may be administered in dyspnoea when morphine is contraindicated. He claims that as the drug does not induce euphoria, there is no likelihood of the habit being developed. In pulmonary phthisis not only was the harassing cough allayed, but the night-sweats were checked and insomnia relieved. Disagreeable effects were rarely observed.

Darier<sup>4</sup> has employed with success 5 per cent. solutions of dionin for instillation into the conjunctival sac or injected beneath the conjunctiva to relieve pain in various ocular affections. By this means he was able to relieve the pain of corneal ulcer and glaucoma.

A. Graefe<sup>5</sup> employed the drug in combination with atropine, and found it of value in iritis and iridocyclitis.

Daxenberger<sup>6</sup> has seen two cases in which severe reaction continued for thirty-six hours after the application of the drug.

<sup>1</sup> Wiener med. Blätter, 1899, Heft 25.

<sup>2</sup> Münch. med. Wochenschr., December, 1899.

<sup>3</sup> Ibid.

<sup>4</sup> La Presse Médicale, April 7, 1900.

<sup>5</sup> Deutsche med. Wochenschr., March 22, 1900.

<sup>6</sup> Wochenschrift f. Therapie und Hygiene des Auges, May 10, 1900.

From these favorable reports we cannot but assume that in dionin we have a drug that gives hopes of great usefulness and will, no doubt, be fully tried and, if found deserving, be extensively used. The following are some of the formulæ that have been suggested :

For chronic bronchitis and pulmonary phthisis :

|                                                              |           |            |
|--------------------------------------------------------------|-----------|------------|
| R.—Dionin . . . . .                                          | g. iij.   | gm. 0.19   |
| Aquæ laurocerasii . . . . .                                  | f ʒ ijss. | c.c. 10.00 |
| Misce. Sig.—Fifteen drops in water two or three times a day. |           |            |

For insomnia with pain :

|                                                         |                   |            |
|---------------------------------------------------------|-------------------|------------|
| R.—Dionin . . . . .                                     | gr. ij.           | gm. 0.125  |
| Sodii bromidi . . . . .                                 | ʒ ij.             | gm. 8.00   |
| Aquæ . . . . .                                          | q. s. ad f ʒ iij. | c.c. 90.00 |
| Misce. Sig.—Two teaspoonfuls in water every four hours. |                   |            |

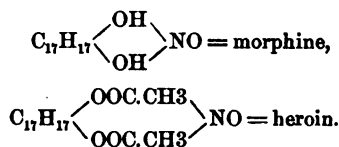
For the relief of pain from gastric ulcer :

|                                           |           |          |
|-------------------------------------------|-----------|----------|
| R.—Dionin . . . . .                       | gr. ijʒ.  | gm. 0.15 |
| Bismuthi subnitratiss . . . . .           | gr. lxxv. | gm. 5.00 |
| Misce et ft. chart. No. x.                |           |          |
| Sig.—One powder four or five times a day. |           |          |

For subacute bronchitis with excessive cough :

|                                                                |                |            |
|----------------------------------------------------------------|----------------|------------|
| R.—Dionin . . . . .                                            | gr. j.         | gm. 0.065  |
| Terpin. hydrat. . . . .                                        | ʒj.            | gm. 4.00   |
| Elix. aromat. . . . .                                          | q. s. f ʒ iij. | c.c. 90.00 |
| Misce. Sig.—One to two teaspoonfuls every three or four hours. |                |            |

**HEROIN.** Heroin, or diacetic ester of morphine, is a white, crystalline, neutral, slightly bitter powder. It is sparingly soluble in water, but is rendered quickly soluble by the addition of a small quantity of dilute acid. With acids it forms salts which are precipitated from aqueous solution by the addition of alkalies. The relation of heroin to morphine may be noted by a comparison of their formulæ :



It will be seen that the latter is morphine in which both HO groups have been replaced by the acetyl radical  $\text{OCCH}_3$ . When first introduced, heroin was given to adults in single doses of  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.01 to 0.02 gm.), but these doses were soon found to be both rather large and unnecessary, and it is now more generally employed in doses of  $\frac{1}{32}$  to  $\frac{1}{16}$  grain (0.0025 to 0.005 gm.) for adults and in proportionately smaller doses for children. The dose for a child is from  $\frac{1}{160}$  to  $\frac{1}{80}$  of a grain ( $\frac{1}{160}$  to 1 mg.). It may be administered in pills, powders, tablets, cap-

sules, or in liquids, but in the latter form a few drops of diluted acetic acid should be added to render it soluble. When used hypodermatically the hydrochlorate, on account of its solubility, should be employed, but allowance should be made for it being a weaker preparation.

This morphine derivative, although previously known and studied, owes its introduction into practical medicine to Dreser and Floret, who, in 1898, made physiological and clinical studies of it and offered it as a substitute for morphine in many of its uses. They claimed that it was free, or comparatively so, from the disagreeable effects of morphine. Floret especially recommended it for the purpose of allaying cough in acute bronchitis and of equal value to morphine for allaying the cough of chronic bronchitis. Many of the later writers have lauded the drug much more highly than its original champions, claiming remarkable effects for it as an analgesic, expectorant, respiratory stimulant, and also as a cure for diabetes mellitus and the opium habit. During the past year many clinical reports have been made upon heroin, and while on extravagant claims have withstood the test of time, the drug has been found to be of value, and will no doubt be accorded a place corresponding to its merit. Wierzbicki<sup>1</sup> was pleased with the action of heroin after using it in seven cases which were carefully studied. In phthisis and bronchitis he found the cough to be eased and expectoration lessened in quantity, the diminution being in the serous but not in the mucopurulent constituents of the sputum. It had no effect upon temperature, circulation, digestion, or upon the night-sweats of tubercular patients. The only after-effect noted was in one patient who experienced dryness in the throat. He experimented upon himself with  $\frac{1}{8}$ -grain (0.02 gm.) doses, and experienced no bad effect except a certain amount of languor, drowsiness, and dryness of the throat. As is well known, these are much the same symptoms experienced by a great many individuals after taking morphine or its salts.

H. Leo,<sup>2</sup> when employing heroin in doses of  $\frac{1}{8}$  of a grain (0.01 gm.), frequently observed nausea, vomiting, and fainting; but when the dose was reduced to  $\frac{1}{16}$  of a grain (0.005 gm.) no ill effects were noticed. In the treatment of dyspnoea his results were most satisfactory, and he considered it a valuable respiratory stimulant, comparing its action upon the respiration to the action of digitalis upon the circulation. In asthma he recommends its combination with potassium iodide, and also speaks highly of it in the treatment of chronic bronchitis and emphysema.

Frudenthal<sup>3</sup> used the drug with good results to relieve the cough of

<sup>1</sup> Klin. Therap. Wochenschr., 1899, No. 27.

<sup>2</sup> Deutsche med. Wochenschr., March 23, 1899.

<sup>3</sup> Philadelphia Medical Journal, March 25, 1899.

pulmonary tuberculosis and chronic bronchitis and also in pseudocroup of children. The doses employed by him were  $\frac{1}{12}$  of a grain (0.005 gm.) three times a day for adults and  $\frac{1}{24}$  of a grain (0.0005 gm.) for children. Constipation resulted in 2 per cent. of the cases in which the drug was employed, and he suggested that small quantities of cascara or aloin should be given with each dose of heroin. In phthisis his results were good in three cases, but in two others failures were reported. In influenza the drug was employed with benefit, and in these cases when complicated by pleurisy it was given in combination with salophen. In two instances he combined apomorphine with heroin. In both the patients suffered with severe dizziness and headache.

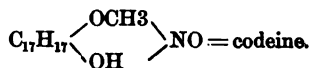
Floret<sup>1</sup> reports a series of cases treated with heroin. He emphasizes its value in allaying cough and otherwise benefiting cases of acute catarrhal bronchitis. He considers it a respiratory stimulant, and in bronchitis sicca attributes much of its benefit to this action. In treating pulmonary phthisis, especially at its beginning, he obtained good results from the following combination :

|           |   |   |   |   |   |          |          |
|-----------|---|---|---|---|---|----------|----------|
| R.—Duotal | . | . | . | . | . | gr. xlv. | gm. 3.00 |
| Heroin    | . | . | . | . | . | gr. ss.  | gm. 0.03 |

Misce et ft. chart. No. vi.

Sig.—One powder three or four times a day.

Erick Harnack,<sup>2</sup> taking into consideration the formula of heroin, the literature referring to its use, and his experiments upon dogs, considers it a more toxic drug than morphine. He claims that certain organic bases, by substitution with acid ethers, and especially by making an acetyl, may become much more toxic than the base in its original form. He does not consider it a fair inference that because codeine is less toxic than morphine heroin also should be less toxic :



To form codeine, a hydroxyl group in morphine is replaced by one methyl radical, while to form heroin from morphine the hydroxyl group is replaced by the more powerful acetyl radical. He opposes Dreser's claims that heroin is less toxic in its effects upon the respiration than morphine, and his experiments upon dogs apparently bear him out in this statement. It must be borne in mind, however, that these animals are affected by opiates in a somewhat different manner from man. The deductions of Harnack, while not convincing, should not be lightly cast aside, and have undoubtedly directed the attention of the profession to the fact that heroin, if given in sufficient doses, is a toxic substance.

<sup>1</sup> Therap. Monatsheft, June, 1899.

<sup>2</sup> Münch. med. Wochenschrift, July 4, 1899.

Karl Mirtl<sup>1</sup> employs tampons soaked with a solution of heroin in the treatment of parametritis and perimetritis and painful diseases of the uterine appendages. Tampons are thoroughly soaked with the following solution :

|                            |               |      |         |
|----------------------------|---------------|------|---------|
| R.—Heroin . . . . .        | gr. xv.       | gm.  | 1.00    |
| Acid. acetici dil. . . . . | Mxxx.         | c.c. | 2.00    |
| Aquæ dest. . . . .         | f℥jss.        | c.c. | 45.00   |
| Glycerini . . . . .        | q. s. ad Oij. | c.c. | 1000.00 |

A well-soaked tampon should hold from  $2\frac{1}{2}$  to 4 drachms (10 to 16 gm.) of this solution, which is equivalent to 0.01 to 0.015 gramme, or  $\frac{1}{8}$  to  $\frac{1}{4}$  grain, of heroin. In cases of severe pain a solution of 1 : 600, that is, 0.015 to 0.025 gramme of heroin in each tampon, was necessary. Some relief from pain was usually obtained in from one-fourth to one-half an hour, and in from one to one and a half hours the pain had entirely subsided. There were no ill effects from the use of the tampon, although the patient frequently complained of languor four to six hours after their application. Suppositories containing  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.01 to 0.015 gm.) may be used instead of tampons.

Solés<sup>2</sup> reports a case of poisoning by heroin in a woman, forty years of age, who had taken by mistake about  $2\frac{1}{2}$  grains (0.16 gramme) at a single dose. He saw her about four hours after the drug had been taken, and found her in a state of great exhaustion, with dimness of vision, active myosis, and trembling of the extremities. The pulse was thready and one hundred and forty to the minute. The temperature was reduced 2° C. After coffee had been administered the patient vomited and there was incontinence of urine. Caffeine was given hypodermatically in the dose of  $1\frac{1}{2}$  grains (0.10 gm.), after which the sight rapidly improved and the patient fell into a quiet sleep.

Max Einhorn<sup>3</sup> used heroin extensively in the treatment of a variety of gastric and pulmonary affections, and to a limited extent in cases of cardiac dyspncea. He recommends it principally on account of its properties of allaying cough and easing respiration, in addition to its general analgesic properties. Except slight dizziness and occasional dryness of the throat, he has not seen unpleasant symptoms even from its prolonged use. In one of his cases there was constipation following its administration. The doses given by him were  $\frac{1}{12}$  of a grain (0.005 gm.) twice a day.

Henry D. Fulton<sup>4</sup> states that maximum doses of heroin produced gastric disturbances similar to those following the administration of

<sup>1</sup> Wiener med. Wochenschr., 1899, No. 25.      <sup>2</sup> Therap. Monatsheft, October, 1899.

<sup>3</sup> Philadelphia Medical Journal, October 28, 1899.

<sup>4</sup> New York Medical Journal, December 30, 1899.



morphine, but in a lesser degree, and by giving moderate doses its desired effects can usually be obtained short of causing any derangement of digestive functions.

Morris Manges<sup>1</sup> reviews the literature concerning heroin, and states that he considers it a valuable drug and preferable to morphine or codeine in many cases. After prolonged use the doses must, as a rule, be somewhat increased. In acute bronchitis not only is the cough, as a rule, promptly relieved, but the whole condition of the patient is quickly improved, while in chronic bronchitis the beneficial effects appear to depend on whether the drug diminishes the bronchial secretion or not. In bronchiectasis, except in those cases where secretion was diminished by its use, the results were good, especially if the patient was placed in a position to permit him to get rid of accumulated secretion by gravity. In pulmonary emphysema he considers it distinctly superior to all other measures. In asthmatic attacks he prefers the use of the hydrochloride, given subcutaneously in doses of from  $\frac{1}{12}$  to  $\frac{1}{8}$  of a grain (0.005 to 0.01 gm.), repeated in an hour if necessary, and after that time in smaller doses by the mouth every six hours, to insure sleep. The largest dose should be reserved for bedtime. Attacks of influenza are shortened and respiratory symptoms are allayed. In whooping-cough the paroxysms are lessened in frequency and severity. Although well borne in these diseases, the doses must be small for children. In pulmonary phthisis, both acute and chronic, he believes the drug to have a wide field of usefulness, and considers it distinctly superior to codeine in most cases and morphine in many. Not only does it allay cough, but he believes it to be a stimulant to respiration, removing the oppressive sensation of dyspnoea, promoting sleep, and frequently lessening or preventing night-sweats, and even at times reducing the evening rise of temperature. In cardiac and renal asthma he has found it inferior to codeine or morphine, although its soothing effects were sufficient for mild attacks. In the treatment of the opium habit he indorses the use of this drug. He has not found it valuable in diabetes mellitus or equal to morphine to relieve the pain of neuralgia. He does not agree with those who assert that the only after-effects from the use of heroin are slight transient vertigo and a little somnolence, or that it is necessary to increase the drug; but, upon the whole, he considers the disagreeable after-effects as much less frequent and milder than those commonly seen after the administration of morphine.

Habituation was noticed in several cases, but no patient suffered from symptoms of chronic morphinism.

<sup>1</sup> New York Medical Journal, January 13 and 20, and February 24, 1900.

Loewenthal<sup>1</sup> employed heroin in doses of from  $\frac{1}{80}$  to  $\frac{1}{128}$  grain (0.0007 to 0.00012 gm.), every three or four hours, with satisfactory results in the treatment of whooping-cough.

Thomson<sup>2</sup> reports two cases in which heroin produced vomiting that continued until the drug was stopped. One case was that of a child, five years old, who had a bad regurgitant murmur and was suffering with whooping-cough. She was given  $\frac{1}{32}$  grain (0.0025 gm.) every five hours. Two days later he was called to see the child, and found her decidedly exhausted, having vomited thirty-six hours, and in spite of active stimulation she died the following day. Manges, in commenting on this case, considers that under the circumstances the doses were excessive. Dr. William J. Robinson reports two cases in which he saw active vomiting as a result of the administration of heroin given in doses of  $\frac{1}{8}$  of a grain (0.01 gm.).

From a review of these papers and from experience obtained in using the drug during the past year, I am convinced that in it we have a valuable agent for the purpose of allaying harassing cough and in many cases inducing sleep, but that in all cases it must be employed with the same discriminating care as other opiates. To obtain its beneficial effect and avoid nausea, vomiting, languor, and constipation it must be given to adults in doses not, as a rule, exceeding  $\frac{1}{24}$  to  $\frac{1}{12}$  grain (0.0025 to 0.0054 gm.) three or four times a day. As an analgesic it is inferior to codeine and morphine, but occasionally may be employed as a substitute for these alkaloids when the latter are not well borne. The drug, however, should not be pushed in these or other cases. Unless moderate doses give the desired relief the use of the drug should be abandoned. In dyspnoea it is not possible to lay down any fixed rules as to the cases most suitable for its use. Small doses frequently relieve mild attacks of dyspnoea in asthma, cardiac dilatation, enfeeblement, and uræmia. As is well known, opiates in these cases are employed with the greatest caution, and in using heroin no exception should be made.

The following are some of the formulæ that have been employed in the treatment of various bronchial and pulmonary conditions calling for sedatives :

To allay cough and promote excretion in subacute and chronic bronchitis :

|                         |        |           |
|-------------------------|--------|-----------|
| R.—Heroin . . . . .     | gr. j. | gm. 0.064 |
| Terpin. hydrat. . . . . | gr. l. | gm. 3.24  |
| Ext. glycyrrh. . . . .  | gr. l. | gm. 3.24  |

Misce et ft. tabellæ compressæ No. xxiv.

Sig.—One tablet every four to six hours during the day.

<sup>1</sup> Philadelphia Medical Journal, September 8, 1900.

<sup>2</sup> New York Medical Journal, February 3, 1900.

|                              |                  |      |        |
|------------------------------|------------------|------|--------|
| R.—Heroin . . . . .          | gr. j.           | gm.  | 0.064  |
| Acidi acet. diluti . . . . . | gtt. x.          | c.c. | 0.60   |
| Ammonii chloridi . . . . .   | ʒ ij.            | gm.  | 8.000  |
| Syrupi lactucarii . . . . .  | ʒj.              | c.c. | 30.000 |
| Aquæ . . . . .               | q. s. ad f ʒ ij. | c.c. | 90.000 |

Misce. Sig.—Shake. One or two teaspoonfuls every six hours.

For asthma or pulmonary emphysema :

|                           |                  |      |        |
|---------------------------|------------------|------|--------|
| R.—Heroin . . . . .       | gr. j.           | gm.  | 0.064  |
| Acidi citrici . . . . .   | gr. xx.          | gm.  | 0.60   |
| Potassii iodidi . . . . . | ʒj.              | gm.  | 4.000  |
| Syr. tolut. . . . .       | f ʒj.            | c.c. | 30.000 |
| Aquæ . . . . .            | q. s. ad f ʒ ij. | c.c. | 90.000 |

Misce. Shake. Sig.—One to two teaspoonfuls in water every four to six hours.

To lessen pain and relieve cough or influenza :

|                     |        |     |       |
|---------------------|--------|-----|-------|
| R.—Heroin . . . . . | gr. j. | gm. | 0.064 |
| Salophen . . . . .  | ʒ ij.  | gm. | 8.000 |

Misce et ft. chart. No. xxiv.

Sig.—One powder three times a day.

For pertussis in a child three years old :

|                             |                  |     |        |
|-----------------------------|------------------|-----|--------|
| R.—Heroin . . . . .         | gr ʒ.            | gm. | 0.0128 |
| Acidi citrici. . . . .      | gr. v.           | gm. | 0.32   |
| Phenazon. . . . .           | gr. xvj.         | gm. | 1.02   |
| Tinct. belladonnæ . . . . . | gtt. xxxij.      | gm. | 2.00   |
| Syrupi . . . . .            | q. s. ad f ʒ iv. | gm. | 120.00 |

Misce. Sig.—Shake. Teaspoonful every six hours.

**Menthol Valerianate** is a colorless liquid of about the consistency of glycerin, having the agreeable odor of mint and a slightly bitter taste. It has been used with good effect by Vertun<sup>1</sup> in doses of from 10 to 15 minims (0.60 to 1 gm.), three times a day, as a sedative in the treatment of chorea, neurasthenia, hysteria, and vesical irritation. It is given in capsules as follows :

|                                    |     |     |      |
|------------------------------------|-----|-----|------|
| R.—Menthol. valerianatis . . . . . | ʒj. | gm. | 4.00 |
|------------------------------------|-----|-----|------|

Pone in capsulas No. xii.

Sig.—One capsule three times a day.

**Methylene-blue.** The value of methylene-blue in the treatment of gonorrhœa and malaria has been firmly established, and it has also been employed with asserted success in the treatment of neuralgia, sciatica, migraine, neuritis, and, to a limited extent, in diabetes mellitus, in which it appears to act in a similar manner to antipyrine. Pietro Bodoni<sup>2</sup> employed it in doses of from  $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.032 to 0.100 gm.) by intramuscular injection upon fourteen patients, and states that it

<sup>1</sup> Berlin. klin. Wochenschr., August 14, 1899.

<sup>2</sup> Klin. Therap. med. Wochenschr., 1899, No. 21, p. 665.

is a distinct nervous sedative, and should be classed with sulphonal, chloretone, hyoscin, bromoform, and other similar substances. The usual dose is from 1 to 2 grains (0.065 to 0.12 gm.) in pills, capsules, or tablets, three times a day, and, if so desired, it may be administered by intramuscular injection.

In normal subjects its elimination by the urine begins in about an hour and continues from twelve to twenty-four hours; but in diseased conditions, when absorption is slow and elimination poor, it is not seen in the urine so soon and persists for a longer time. Sometimes nausea, vomiting, or purging are seen after the administration of methylene-blue, but one of its most frequent untoward effects is vesical irritation, many persons being very susceptible in this respect, even when small doses are given. In renal congestion or inflammation, when elimination is interfered with, the drug accumulates in the organism and the sclera and skin become blue. J. W. P. Smithwick<sup>1</sup> considers methylene-blue a valuable substitute for quinine in the treatment of malaria of every form and under all conditions. In his paper he gives a table of different types of the disease in which methylene-blue was employed with satisfactory results. Of these there were twenty-four cases of quotidian, four of tertian, three of quartan, five of æstivo-autumnal, three of hemorrhagic, and one of double quotidian malarial fever. Three of the patients refused to continue the treatment after the first day on account of the deep blue color of the urine, which always appears when the drug is administered, and four others died from organic diseases. He believes the drug to be superior to quinine in the treatment of hemorrhagic forms of malaria occurring during pregnancy and in persons who have an idiosyncrasy to quinine.

During the past year considerable experimental work has been carried on with methylene-blue in testing the rapidity of absorption and elimination, and also the permeability of the kidneys in different diseased conditions by F. Widal,<sup>2</sup> Müller,<sup>3</sup> Renon and Latron,<sup>4</sup> also Achard and Clerc.<sup>5</sup> A note of warning is sounded by Michailow against the indiscriminate use in large and continued doses of methylene-blue. From his laboratory researches carried out on healthy animals he found that it produced marked changes in the tissues and organs.

As much of the methylene-blue found in the market is contaminated with zinc and other impurities, care should be taken when giving the drug internally to select a chemically pure article :

<sup>1</sup> Merck's Archives, February, 1900.

<sup>2</sup> Bull. de la Soc. de Méd. des Hôpitaux de Paris, April 5, 1900.

<sup>3</sup> Deutsch. Arch. f. klin. Med., May 30, 1899.

<sup>4</sup> Medical News, September 1, 1900, p. 349.

<sup>5</sup> La Presse Médicale, February 10, 1900.

|                                 |           |          |
|---------------------------------|-----------|----------|
| R.—Methylene-blue (C. P.) . . . | gr. xxiv. | gm. 1.60 |
| Sacchari lactis . . . . .       | 3j.       | gm. 4.00 |
| Alcohol . . . . .               | q. s.     |          |

Misce et ft. tabellæ trit. No. xxiv.

Sig.—One tablet three times a day.

|                                 |           |          |
|---------------------------------|-----------|----------|
| R.—Methylene-blue (C. P.) . . . | gr. xxiv. | gm. 1.60 |
| Petrolati spissi . . . . .      | gr. xxx.  | gm. 2.00 |
| Ext. glycyrrh. . . . .          | gr. xxx.  | gm. 2.00 |

Misce et ft. pil. (or caps.) No. xxiv.

Sig.—One pill (capsule) three times a day.

A good combination in malaria is as follows :

|                                 |          |          |
|---------------------------------|----------|----------|
| R.—Methylene-blue (C. P.) . . . | gr. xxv. | gm. 1.06 |
| Duotal . . . . .                | gr. c.   | gm. 6.00 |

Misce et ft. caps. No. xxv.

Sig.—One capsule three times a day.

**Nirvanin.** This synthetical product is chemically related to orthoform, and appears in white crystals which are freely soluble in water. It has been employed as a local anæsthetic upon mucous membranes, and also as a local anæsthetic in subcutaneous injections in the strength of from 2 to 5 per cent. in physiological salt solution. Luxenburger<sup>1</sup> claims that the drug is only one-tenth as poisonous as cocaine, and employed it to produce satisfactory anæsthesia in performing ninety-four operations. Bolognesi<sup>2</sup> asserts that the drug being far less toxic than cocaine, may be employed in greater quantities by subcutaneous injection for the purpose of producing local anæsthesia. Charles A. Elsberg<sup>3</sup> concludes from his experiments that nirvanin has distinct anæsthetic properties when used subcutaneously, and is ten times less poisonous than cocaine and more than three times less poisonous than eucaine. It is a stable compound, and may be boiled without diminishing its anæsthetic properties.

C. F. Floeckinger<sup>4</sup> states that nirvanin possesses the following advantages over cocaine: It is less toxic; it is anti-bactericidal; its anæsthetic effects appear earlier and are more prolonged, and there is no danger of setting up a drug habit. Furthermore, the pain which always follows the use of cocaine after its anæsthetic effect passes off is absent when nirvanin injections are properly employed. Scrini and Artault<sup>5</sup> are less favorably impressed with nirvanin, and found from experiments performed upon the eyes of rabbits and men that it was irritating and uncertain in its effect, and that the period of anæsthesia was of brief duration. Furthermore, solutions of the drug rapidly be-

<sup>1</sup> Münch. med. Wochenschr., 1899, No. 2.

<sup>2</sup> Bull. Gén. Thérap. Méd., December, 1899.

<sup>3</sup> New York Medical Journal, January 13, 1900.

<sup>4</sup> New Yorker Monatschrift, June, 1900.

<sup>5</sup> Arch. d'Ophtal., December, 1899.

come infected. V. K. Diedrichson,<sup>1</sup> after experimenting with nirvanin upon animals, states that it is by no means a harmless substance, and that the dose should be regulated with more care than is done by many authors. The following prescription is suitable for the purpose of producing local anæsthesia upon mucous membrane or for subcutaneous injection :

|                                   |         |          |
|-----------------------------------|---------|----------|
| R.—Nirvanin . . . . .             | gr. ij. | gm. 0.13 |
| Sodii chloridi . . . . .          | gr. j.  | gm. 0.06 |
| Aquæ destil. (sterilized) . . . . | f ʒ ij. | gm. 8.00 |

Misce.

**Orphol**, or basic bismuth betanaphтол, is a light red-brown, insoluble powder. It is employed as an astringent and antiseptic in the treatment of diarrhœa. It is claimed that it passes through the stomach unchanged, but in the intestine splits up into its component parts. Its dose for adults is from 15 to 20 grains (1 to 1.3 gm.) and for children from 2 to 5 grains (0.125 to 0.3 gm.), to be administered either in powder or in liquid suspended by mucilaginous substances.

|                          |                   |            |
|--------------------------|-------------------|------------|
| R.—Orphol . . . . .      | ʒj.               | gm. 4.00   |
| Acacie . . . . .         | ʒj.               | gm. 4.00   |
| Aquæ cinnamoni . . . . . | q. s. ad f ʒ iij. | c.c. 90.00 |

Misce. Sig.—Shake well, and take one teaspoonful every three hours.

Each drachm of the above prescription contains  $2\frac{1}{2}$  grains (0.15 gm.) of orphol.

**Orthoform**. This synthetic compound has now been employed for a sufficient length of time to enable us to judge of its value and know its limitations. Although soluble in ether, it is practically insoluble in water, and therefore when applied even in large quantities for a long period of time there is little danger of producing toxic effect through absorption. Untoward effects, however, have been observed in some cases where the nutrition of the tissues was poor or the patient was thought to have an idiosyncrasy to the drug. Upon the other hand, it has been employed every day for months in large quantities without producing any untoward effects. On account of its insolubility in water it cannot conveniently be employed hypodermatically, but, if so desired, it may be suspended in oil and injected subcutaneously. The drug has little or no anæsthetic effect upon the intact skin or mucous membrane, but its special advantage over all local anæsthetics is that when applied in 10 to 20 per cent. ointments or as a dusting powder to open wounds and ulcers anæsthesia comes on in a few moments and persists for from two to three hours. Its antiseptic properties are about the same as boric acid, and are probably too feeble to permit of its practical application for this purpose. Untoward effects following the application of ortho-

<sup>1</sup> *Wratch*, May 25, 1900.

form have been observed by Wunderlich,<sup>1</sup> Katz,<sup>2</sup> and Brocq.<sup>3</sup> In Wunderlich's cases the untoward effects were not produced when the drug was used in the form of a powder, while Katz was uncertain as to whether the untoward effects were to be attributed to the deleterious effects upon the orthoform by the tin with which it had been in contact for some time, whether the drug had undergone decomposition from being so long kept, or to the idiosyncrasy of the patient. Luxenburger<sup>4</sup> found orthoform to be compatible with iodoform, dermatol, urophen, aristol, calomel, salicylic acid, carbolic acid, lysol, lead water, boric acid, alumen-acetate, ichthyol, turpentine, iodine and copper sulphate. Chemical changes take place in bismuth subnitrate, potassium permanganate, and silver nitrate when combined with orthoform, and precipitation results when combined with bichloride of mercury or formaldehyde. Antipyrine triturated with orthoform is converted into a semi-liquid. The drug is employed to relieve the pain of ulcers, severe burns, fissures of the nipple and anus, to relieve the pain of cancer, by irrigation in painful cystitis, and also very widely in aural, ophthalmic, and laryngological practice. In severe gastralgia and in simple or cancerous ulcers of the stomach  $7\frac{1}{2}$  to 15 grains (0.50 to 1 gm.) may be administered by the mouth once or twice daily for the purpose of relieving the pain. The following formula may be found convenient :

|                          |        |      |       |
|--------------------------|--------|------|-------|
| R.—Orthoform . . . . .   | gr. l. | gm.  | 3.03  |
| Syrupis acaciæ . . . . . | 3 ij.  | c.c. | 60.00 |

Misce. Sig.—Shake well, and take from two to four teaspoonfuls once or twice a day.

In painful fissures of the nipple powdered orthoform has been found to be of the greatest value, but when pain exists without open wounds the powder cannot enter, and may be substituted by the following mixture of Bardet :

|                                |           |      |       |
|--------------------------------|-----------|------|-------|
| R.—Orthoform . . . . .         | gr. lxxv. | gm.  | 5.00  |
| Ether, q. s. ad sol.           |           |      |       |
| Olei amygdalæ expressi . . . . | 3 v.      | c.c. | 20.00 |

Misce. Sig.—External use.

The nipple should be thoroughly washed with 20 per cent. alcohol in water each time before nursing the child, to avoid intoxication of the nursing. For dry, excoriated hemorrhoids Bardet gives the following prescription to relieve pain :

|                       |         |     |       |
|-----------------------|---------|-----|-------|
| R.—Zinci oxidi,       |         |     |       |
| Olei olivæ,           |         |     |       |
| Cerati albe . . . . . | aa 3 v. | gm. | 20.00 |
| Balsam Peruv. . . . . | gr. x.  | gm. | 0.60  |
| Orthoform . . . . .   | 3 ijss. | gm. | 10.00 |

Misce. Sig.—Apply several times a day.

<sup>1</sup> Münch. med. Wochenschr., October 3, 1899.

<sup>2</sup> Ibid., May 15, 1899.

<sup>3</sup> La Presse Médicale, April 18, 1899.

<sup>4</sup> Münch. med. Wochen., January 9, 1900.

Loza gives the following formula, to be employed hypodermatically in the treatment of syphilis :

|                        |           |              |
|------------------------|-----------|--------------|
| R.—Petrolati (liquid)  | . . . . . | gr. cl.      |
| Hydrarg. chlorid. mite | . . . . . | gr. lxvijsa. |
| Orthoform              | . . . . . | gr. xij.     |

Misce. Sig.—Dose, fifteen to thirty drops.

**Ovarian Extract.** This substance has been employed to a limited extent in the treatment of the nervous symptoms which appear at the time of the menopause, amenorrhœa, and dysmenorrhœa. The exact cases in which it is indicated are not definitely known. Toulouse and Marchand<sup>1</sup> report several cases of epilepsy with suppression of menstruation in which the function was restored, and the periods between the epileptic attacks were lengthened during the administration of ovarian extract. The dose of the extract is from 5 to 15 grains (0.32 to 1 gm.) daily.

|                           |           |      |           |
|---------------------------|-----------|------|-----------|
| R.—Opoovarinii            | . . . . . | ℥iv. | gm. 16.00 |
| Fiant tabellæ No. xlviii. |           |      |           |

Sig.—One to two tablets three times a day.

**Oxycamphor, or Oxyphor.** This is a white, crystalline substance, sparingly soluble in water, but freely soluble in alcohol, and is to be obtained in the market in a 50 per cent. alcoholic solution under the name of oxyphor. It is said to be a sedative to the respiratory centre, to the central nervous system, and a mild stimulant to the circulation. It has been employed for the relief of dyspnœa, in pulmonary tuberculosis, in asthma, and also in cardiac and uræmic dyspnœa. Ehrlich<sup>2</sup> employed the drug as a respiratory sedative in dyspnœa of advanced phthisis and in cardiac dyspnœa, and found that it not only proved valuable as a respiratory sedative, but that quiet sleep and free diuresis followed its use. He gives the following formula :

|                    |           |        |             |
|--------------------|-----------|--------|-------------|
| R.—Oxyphor         | . . . . . | ℥ijss. | gm. 10.00   |
| Alcohol            | . . . . . | f℥j.   | c.c. 30.00  |
| Syr. aurant. cort. | . . . . . | f℥v.   | c.c. 20.00  |
| Aquæ dest.         | . . . . . | f℥v.   | c.c. 150.00 |

Misce. Sig.—One teaspoonful three or four times a day.

Each teaspoonful of the above mixture contains 1 gramme (15 grains) of the drug.

Oxycamphor may be given in compressed tablets or in alcohol solution, in doses of from 5 to 20 grains (0.30 to 1.30 gm.) three times a day.

|                                            |           |      |          |
|--------------------------------------------|-----------|------|----------|
| R.—Oxycamphoræ                             | . . . . . | ℥ij. | gm. 8.00 |
| Fiant. tabellæ compressæ No. xxiv.         |           |      |          |
| Sig.—One tablet every three or four hours. |           |      |          |

<sup>1</sup> La Gynécologie, June 15, 1900.

<sup>2</sup> Centralblatt f. Gess. Therapie, 1899, Heft 1.



Jacobsohn<sup>1</sup> also employed the drug with good effect in respiratory and cardiac dyspnoea, but found in some instances, after the patient became accustomed to its use, it no longer acted satisfactorily. In two cases of bronchial asthma in which I employed the drug it appeared to give temporary relief.

**Palladium Chloride.** This salt of palladium has been employed by S. Solis Cohen<sup>2</sup> in the treatment of phthisis. Seventy-five per cent. of the cases improved, the appetite increased, there was improvement in weight, and in some the fever and cough disappeared, and physical examination showed that the stricture lesions in the lung were much less demonstrable. The following prescription was found to be a convenient method of administration :

|                                                               |             |      |       |
|---------------------------------------------------------------|-------------|------|-------|
| R.—Palladii chloridi . . . . .                                | gr. xv.     | gm.  | 1.00  |
| Acid. hydrochlor. dil., q. s. ad sol.                         |             |      |       |
| Aque dest. . . . .                                            | q. s. f ʒj. | c.c. | 30.00 |
| Misce. Sig.—Five drops in half a glass of water before meals. |             |      |       |

In most of the cases the remedy was continued for a long time, and the initial dose of five drops was gradually increased in some cases to ten drops. In several neurotic subjects the larger doses produced circulatory excitement, and in some cases better results were obtained by alternating with iodoform for a few days at a time.

**Parotid Gland.** The desiccated parotid gland of sheep, in the form of tablets, each representing about four grains of the fresh gland, have been employed by John B. Shober<sup>3</sup> in the treatment of so-called ovarian neuralgia and of dysmenorrhœa unassociated with extensive inflammatory disease. The doses employed are from two to six tablets daily, and in properly selected cases he states that remarkable results and cures in a few weeks have followed its use in patients who had previously suffered for years. He emphasizes the fact that the gland is not a "cure-all," and that it will not bring about a cure in hydrosalpinx or pyosalpinx in which the ovaries are bound down and adherent and in which the tubes are chronically inflamed and thickened. Even in such severe cases, however, he has found that the remedy will usually relieve the pain, but is without effect upon the gross structural changes. These are operative cases, and nothing is to be gained by temporizing.

**Petroleum.** Despite the results of Dixon and Randolph, who proved experimentally that when administered by the mouth fluid petroleum passed through the intestinal tract unchanged and unabsorbed, and that the whole quantity taken could be separated from the stools, favorable results have been reported from time to time by different observers who

<sup>1</sup> Berlin. klin. Wochenschr., 1899, No. 16.

<sup>2</sup> Transactions of the Philadelphia Medical Society, December, 1899.

<sup>3</sup> Journal of the American Medical Association, July 28, 1900.

have employed the substance in the treatment of tuberculosis. William Duffield Robinson<sup>1</sup> confirmed the results of Dixon and Randolph that petroleum passed through the intestinal tract unchanged, and reports fifty selected cases where nutrition, digestion, and body-weight were impaired, and in which in every instance after administering two-drachm doses four times a day for a period of from three to six months there was an increase in weight and improvement in health and strength. The increase in weight was from five and a half to twenty-three and a half pounds. He believes the action of petroleum to be entirely mechanical, and its constant presence in the intestines mechanically influences the growth of micro-organisms. Fermentation and putrefaction are controlled, and the normal functions of the whole intestinal tract are re-established.

**Petrosulfol** is a new bituminous product resembling ichthyol, and owes its medicinal effects to compounds of sulphur, which it contains in large quantities. It has been employed in the treatment of eczema, particularly in dry form, and also in sycosis, furunculosis, and erysipelas. The following formula is considered by S. Ehrmann as best suitable for local application :

|                           |      |     |       |
|---------------------------|------|-----|-------|
| R.—Petrosulfol . . . . .  | 3j.  | gm. | 4.00  |
| Unguenti casein . . . . . | 3iv. | gm. | 20.00 |

Misce. Sig.—For local application.

Another formula that may be used is as follows :

|                          |        |     |       |
|--------------------------|--------|-----|-------|
| R.—Petrosulfol . . . . . | 3jss.  | gm. | 6.00  |
| Lanolin . . . . .        | 3iv.   | gm. | 20.00 |
| Vaseline . . . . .       | 3iv.   | gm. | 20.00 |
| Zinci oxidi . . . . .    | 3ijss. | gm. | 10.00 |
| Pulv. amyli . . . . .    | 3ijss. | gm. | 20.00 |

Misce.—Spread upon gauze and apply to the affected part.

**Phosphorus.** In the treatment of rickets Morse<sup>2</sup> failed to obtain satisfactory results from the use of phosphorus. The doses employed were from  $\frac{1}{160}$  to  $\frac{1}{80}$  grain three times a day. Kassowitz claims that beneficial results were noticeable and rapid from the administration of full doses of phosphorus three times a day and continued for a long time. In the treatment of 560 cases of rickets with this drug deformities and other characteristic symptoms speedily disappeared. The formulæ employed by him were as follows :

|                        |          |      |        |
|------------------------|----------|------|--------|
| R.—Phosphori . . . . . | gr. ss.  | gm.  | 0.0032 |
| Olei morrhue . . . . . | f 3 iij. | c.c. | 90.00  |

Misce. Sig.—Teaspoonful twice daily.

<sup>1</sup> Medical News, July 14, 1900.

<sup>2</sup> Philadelphia Medical Journal, May 26, 1900.

Or the following :

|                               |         |      |        |
|-------------------------------|---------|------|--------|
| R.—Phosphori . . . . .        | gr. ss. | gm.  | 0.0032 |
| Ol. amygdalæ dulcis . . . . . | f ʒj.   | c.c. | 30.00  |
| Pulv. acaciæ . . . . .        | ʒss.    | gm.  | 15.00  |
| Pulv. sacchari . . . . .      | ʒss.    | gm.  | 15.00  |
| Aquæ dest. . . . .            | f ʒjss. | c.c. | 45.00  |

Misce. Sig.—Shake well and give a teaspoonful once, twice, or thrice daily.

It will be observed that each teaspoonful in each of the above prescriptions contains  $\frac{1}{8}$  of a grain of phosphorus. Oil in the prescriptions probably exerts a twofold effect: in the first place, on account of its nutritive value, and, secondly, it assists in the ready absorption of the phosphorus. We have heretofore preferred the U. S. P. elixir of phosphorus, of which each teaspoonful contains  $\frac{1}{4}$  of a grain of phosphorus, on account of its agreeable taste, to all other preparations; but the prescriptions of Kassowitz impress us as being a more rational method of administration. From his experiments upon dogs Lange<sup>1</sup> believes phosphorus will be found to be one of our most reliable remedies in the treatment of convulsions of childhood. After administering it in small doses to a young dog for six days he gave subcutaneous injections of strychnine. The animal developed mild tetanic symptoms, from which it recovered in twenty minutes without other treatment. To another dog of about the same weight and taken from the same litter he gave a smaller dose of strychnine. The animal immediately developed severe tetanic convulsions, and could be kept alive only by the inhalation of an anæsthetic. He claims that phosphorus in about the same doses in which it is used in rickets exercises a more sedative effect upon the nervous system in cases of infantile eclampsia than chloral or bromides. Von Stubenrauch, of Munich, in discussing before the German Surgical Congress at Berlin, 1899, the effect of phosphorus on growing bones, gave the results of his experiments upon the bone-growth in chickens, pigeons, and guinea-pigs. A somewhat firmer growth was noticed in epiphyseal cartilage, depending upon the period of development of the animal, upon the dose of phosphorus, and the time for which it was administered. Contrary to the statements made by other investigators, he asserts that closure of the medullary cavity does not occur. Photographs were exhibited of workers in phosphorus which showed definite bony deposits.

**Prototherapy.** The bactericidal effect of direct sunlight is well established, and it has long been known that it is capable of killing tubercle bacilli and other micro-organisms exposed to it. Its penetrating power is feeble, and its heat rays, if concentrated, are destruc-

<sup>1</sup> Münch. med. Wochenschr., January, 1900.

tive to normal tissues. It remained for Finsen, of Copenhagen, to construct an apparatus so arranged as to exclude the heat rays and concentrate the chemical rays and increase their penetrating and bactericidal power. The method of Finsen, described by Bie,<sup>1</sup> depends for its therapeutic value upon the bactericidal, inflammatory, and penetrating power of the chemical rays upon the skin or mucous membrane exposed to them. Finsen has devised an apparatus through which the light may be filtered and concentrated so as to obtain the full effect of the blue, violet, and ultra-violet rays, the latter of which are most powerful. To prevent burning and to permit penetration of the tissue exposed to their action, arrangements are made for cooling the rays and for rendering the skin or mucous membrane anæmic. For the purpose of concentrating the light lenses are employed, and for cooling such light the space between the lenses of a plain and curved glass is filled with a solution of weak, bright blue ammoniated solution of copper. An apparatus is also described for employing electric light. The method of Finsen has been employed in the treatment of lupus vulgaris, lupus erythematosus, and alopecia areata. Bie reports 350 cases of lupus vulgaris, the greater number of which were treated by the method with satisfactory results. Cures can be effected only upon the skin, hard palate, tongue, and mucous membrane of the cheek and the front part of the nasal septum. Reddening and swelling occur, and sometimes bullæ appear during the course of the treatment, but he has never observed necrosis. In mild cases the light treatment alone is employed, but in severe cases the treatment is supplemented by the application of pyrogallic ointment before the light treatment is applied. Crusts are removed by poultices or by the application of boric-acid solutions, and when the mucous membrane is to be treated the ulcers are touched with a solution of iodide, potassium iodide, or with galvanocautery. The treatment is painless, and Bie states that it has been found certain and constant, and relapses infrequent. In lupus erythematosus the results have not been so favorable as in lupus vulgaris, but cures have been effected in many cases. A few cases have improved very slowly, with constant tendency to recur. Upon the limited number of cases of alopecia areata which had been treated at the time of Bie's report the results had proven most satisfactory. The treatment can be applied only to a small area (1.5 cm.) for an hour each day. O. Lassar,<sup>2</sup> of Berlin, visited Copenhagen to investigate the results obtained by Finsen's method, and is most enthusiastic in his praises. He says: "All doubt regarding the inefficiency of the treatment vanishes at the first sight of the normal faces of the transformed lupus subjects. The disease can be cured by the method, but it is tedious, and requires patience

<sup>1</sup> British Medical Journal, December 30, 1899.

<sup>2</sup> Derm. Zeit., December, 1899.

and persistence." George G. Hopkins<sup>1</sup> describes and illustrates the form of apparatus he employed in phototherapy after the manner of Finsen.

**Picric Acid.** One of the most valuable uses of picric acid is in its application in the treatment of superficial burns. It may be used by applying 1 per cent. aqueous or hydro-alcoholic solution by means of a soft brush, care being observed to preserve the epidermis.

MacDonald's method is to apply gauze moistened with a saturated solution of the acid, covered with absorbent cotton or wool and held in place by a light bandage. The treatment is said to be contraindicated in infants and also for old, suppurating, and deep burns. The advantages claimed for this treatment are its simple method of application, its painlessness, and the rapidity with which healing takes place. Delebecque<sup>2</sup> is favorably impressed with the results obtained by him in the treatment of herpes zoster by applying on absorbent cotton saturated with a 2 per cent. solution of picric acid. The whole should be covered by a gauze dressing held in place by a bandage. The dressing should be renewed every three or four days. By this treatment the intense itching and neuralgic pain are prevented and the ulcers rapidly healed. Hawthorne<sup>3</sup> obtained satisfactory results in the treatment of chancroidal ulcers by applying a saturated solution of picric acid. Care should be observed not to touch the healthy teguments of the penis with the solution, as the tissues become hardened, desquamated, and prurigo erythema follows.

Denos and Guillon<sup>4</sup> used picric acid in solution of from 1 to 200 to 1 to 100 in the treatment of chronic urethritis. In the treatment of anterior urethritis 20 to 80 drops are instilled into the urethra by means of a syringe, to which is adjusted a hard catheter with fine lumen, passed back to but not beyond the compressor urini, and a few drops instilled. They employed the treatment in twenty-nine cases of chronic urethritis, twelve of which were shown to be tubercular and the others due to other micro-organisms. The duration of the treatment was from two weeks to five months, but as a general rule seventeen treatments are sufficient to effect a cure. Of seventeen cases of simple chronic urethritis they obtained definite cures in thirteen cases. Two cases were markedly benefited and in two there were no results. Of the tubercular cases two were cured, seven decidedly improved, two became worse, and one showed no effect.

**Pilocarpin.** A new use of an old drug is the application of pilocarpin to the treatment of biliary diseases. Popham<sup>5</sup> resorts to hypo-

<sup>1</sup> Philadelphia Medical Journal, December 9, 1899.

<sup>2</sup> Revue de Thérap., 1899, No. 20.

<sup>3</sup> La Presse Médicale, May 19, 1900.

<sup>4</sup> Journal de Médecine de Paris, 1899, No. 41.

<sup>5</sup> British Medical Journal, June 30, 1900.

dermatic injections of pilocarpin in ascending doses, and regards the drug of greater value in the treatment of biliary colic than morphine. He believes that the good results obtained are due to the increased secretion in the biliary duct, thereby lubricating the duct and rendering the passage of the stone less difficult.

**Potassium Chlorate.** S. J. Meltzer<sup>1</sup> reviews the literature of the experimental work which has been done to determine the cause of toxic effects shown by potassium chlorate. He does not believe that it has been proven that death results either from disorganization of the blood, inflammation of gastro-intestinal or genito-urinary tract, or from the depressing effect of the drug upon the heart. In view of the effects proven by Roux and Borell, that certain substances act much more powerfully and rapidly when injected into the brain, due to their selective affinity for the nerve cells, and noting that convulsions were of frequent occurrence in many cases of poison from chlorate of potassium, in his experiments upon rabbits he employed intracerebral injections of potassium chloride. When three minims of a 5 per cent. solution were injected into the brain, in most instances tetanic convulsions appeared almost immediately and were followed after a time by clonic convulsions of the extremities. In some instances the animals died in tetanic convulsions. Sometimes death followed by a gradual cessation of respiration, while in other instances the intervals between the convulsions became longer and longer until they entirely ceased, and the animal would lie upon its side for hours with reflexes entirely abolished. When stronger solutions were employed the animal succumbed to the attack in a shorter time, either dying in violent tetanic convulsions or in a state of coma following the convulsion. When a very dilute solution is injected in small quantities the animal runs about incessantly for an hour or more, then falls exhausted in a paretic state, which lasts for a few hours. On the following day the animal appears to be in its normal condition. Sodium chlorate gave rise to the same set of symptoms, but more concentrated solutions are required. His conclusions are that potassium chlorate exercises a powerful toxic effect upon the nerve cells, which are first exhausted and then paralyzed by it.

**Resaldol** is a condensation product of resorcin and saloform. It is insoluble in water, but freely soluble in alkalis. It is said to decompose in the intestinal tract into salicylic acid and resorcin, and, in doses of from 5 to 20 grains (0.30 to 1.30 gm.) three times a day, has been employed in the treatment of diarrhoea with intestinal fermentation. Hermann<sup>2</sup> reports satisfactory results from its use in infectious diseases. He states that in cases of enterocolitis, chronic colitis, and intestinal

<sup>1</sup> Therapeutic Gazette, July, 1900.

<sup>2</sup> Therap. Monatsheft, April, 1900, p. 99.

tuberculosis marked beneficial effects were obtained, but it had little or no beneficial effect in typhoid fever.

R.—Resaldol . . . . . 3ij. gm. 8.00

Pone in cachetas No. xii.

Sig.—One cachet three times a day.

**Salol.** Having noted the beneficial effects obtained by the external use of salol in the treatment of various forms of inflammation of the skin, and particularly its pain-relieving properties, Charles Begg<sup>1</sup> was led to administer it internally in the treatment of smallpox by the systematic use of about 15 grains (1 gm.) three or four times a day. The patients were entirely relieved of all sense of irritation of the skin, and did not have the slightest desire to scratch. When employed early maturation of the vesicles was prevented, except a few isolated vesicles which matured in the usual way. He records a case of confluent smallpox in which by the use of the drug maturation was prevented except in two groups of vesicles which suppurated with greater energy than usual. All the other vesicles dried up without suppurating, and relief from itching was most marked. The treatment suggested by Begg has been resorted to by John Bernacki and P. Napier Jones<sup>2</sup> in the treatment of eight cases of smallpox which had not been previously vaccinated. They found that salol may directly avert general pustulation and even have a partial abortive effect when given after maturation has begun. It almost always interferes with pustulation, and cutaneous inflammation is slight. Irritation of the skin is prevented and unpleasant odor is absent. There is little or no scarring, and the secondary fever is so mild as to be of little importance.

The drug also relieves the itching from jaundice, and might be found valuable in relieving the pain and itching which is sometimes severe in the pustule after vaccination.

**Serum, Sanarelli's.** Until the bacillus *icteroides* is definitely determined to be the cause of yellow fever, little progress can be expected from the use of Sanarelli's serum in the treatment of yellow fever. Sanarelli's reports upon the treatment in two series of cases in Rio Janeiro and San Carlos, in which the mortality in the first instance was 27 per cent. and in the second 33 per cent., are not encouraging. A. Matienzo<sup>3</sup> reports a test of the Doty-Fitzpatrick serum, which is made essentially by the process of Sanarelli, upon six cases of yellow fever, in which the mortality was 50 per cent. In spite of the fact that it was used both subcutaneously and intravenously, the severity of the disease was not modified. Little has transpired since the review of this

<sup>1</sup> British Medical Journal, January 6, 1900.

<sup>2</sup> Ibid., June 2, 1900.

<sup>3</sup> Medical News, January 13, 1900.

subject by Thayer<sup>1</sup> to reconcile the diametrically opposite view of Sanarelli and those who oppose his claims that the bacillus icteroides is the specific cause of yellow fever. In the report of the Commission of Medical Officers of the United States Marine Hospital,<sup>2</sup> working at Havana, it is stated that the bacillus icteroides is the specific cause of yellow fever, that they found the micro-organism in the blood of thirteen out of fourteen cases of the disease examined, and that they did not find or know of any instance where it had been found in persons suffering with any other disease. They found a large number of different animals affected in the same manner and to the same degree by inoculations with the bacillus icteroides, bacillus of Sternberg's colon bacillus, and Havelberg's bacillus and their toxins; but Sanarelli's bacillus was the only one with which they were able to establish a "natural specificity," that is, it was the only micro-organism found to be infectious under natural conditions. Aristides Agramonte<sup>3</sup> criticises the technique of the Commission of Medical Officers of the United States Marine Hospital, and differs with them in their most important statements. He did not find the bacillus icteroides in more than 33 per cent. of cases of undoubted yellow fever, while he did frequently find the bacillus in the blood of persons dying from other diseases. Agramonte also reported four cases of yellow fever treated by subcutaneous injections of the serum from patients convalescent from the disease. None of the patients injected had passed the fourth day of the disease, and in all its course was decidedly modified by the injections, and all recovered. This, of course, while encouraging, is too small a number of cases upon which to base an opinion as to the value of such a serum.

**Serum, Antistreptococcic.** The exact therapeutic value of antistreptococcic serum, as first prepared by Marmorek by immunizing horses with the streptococcus and its products, is far from being definitely settled, but we are at least in a position to better indicate the cases in which it is suitable to use it. All that Marmorek claimed for this serum was that it would be of value in freeing from the tissues the antistreptococci and relieving the symptoms resulting from their toxins. While this statement in general will be found to be correct, there are cases of puerperal sepsis in which there are infectious clots in the uterine sinuses and vessels which it is impossible to reach through the blood-current, and in which no result can be expected except through surgical intervention. George W. Coe,<sup>4</sup> of Chicago, continues to employ the serum with most favorable results. He holds that the disap-

<sup>1</sup> PROGRESSIVE MEDICINE, March, 1899, p. 396.

<sup>2</sup> Public Health Report, August 18, 1899.

<sup>3</sup> Medical News, February 10, 1900.

<sup>4</sup> Journal of the American Medical Association, September 9, 1899.



pointment sometimes expressed after the use of the serum is due principally to one of two reasons: first, many of the sera upon the market are entirely unreliable and not to be compared in therapeutic effect to the serum prepared by Marmorek; secondly, sufficient care has not been taken to differentiate between cases of pure streptococcal infection and cases of mixed infection in which there chances to be streptococci. If the case is one of multi-infection in which the symptoms are due to the predominance of streptococci the serum can be relied upon to combat the symptoms resulting from this micro-organism; but it must not be expected that it will in any degree relieve the symptoms resulting from other infecting organisms. W. E. Macharg,<sup>1</sup> in an analysis of fifty-seven cases of puerperal infection in the Belvidere Fever Hospital at Glasgow, states that the antistreptococcus serum was used upon nine patients. Seven were pure streptococcus infection and two mixed infection of streptococcus and bacillus coli. In six of these there was no apparent result. In the three remaining (one of which died) there was a slight fall of temperature, the result in one was doubtful, and one distinctly improved. Six of the nine died. The dose in these cases was from 10 to 30 c.c. of serum injected into the abdominal wall, repeated at intervals of twelve hours. Dr. Howard Lilienthal<sup>2</sup> advises the use of the serum when the streptococci are found. He insists upon the examination of the blood in all cases in which the serum is used, to determine whether the case is one of true sepsis or not, and, with Egge, agrees that the reports of the use of the serum are valueless unless this precaution has been observed. He also calls attention to the importance of examining the urine and discharges from the womb for streptococci. While advising the use of the serum when streptococci are found in the urine and blood, and in all severe cases of streptococcus infection, he states that he has never observed a case of recovery when the streptococci had been demonstrated in the blood, and that the efficiency of the serum as now prepared had not been proven. Several cases in which there were clinical symptoms of the severest type of sepsis seemed to yield to the serum treatment instituted before it was possible to make an active diagnosis, but they all turned out to be either staphylococcus infection or local streptococcus infection with constitutional symptoms, with no bacteria in the blood. He advises the use of streptococcus serum most strongly in the presence of symptoms of infection by living streptococci, although aware of the fact that the prognosis in these cases is still grave. J. Chalmers Da Costa<sup>3</sup> calls attention to two severe cases of streptococcus infection which were

<sup>1</sup> British Medical Journal, February 17, 1900.

<sup>2</sup> Journal of the American Medical Association, April 14, 1900.

<sup>3</sup> PROGRESSIVE MEDICINE, March, 1900, p. 126.

greatly benefited by the use of the serum. Herbert R. Spencer<sup>1</sup> expresses little confidence in the value of the serum in the treatment of puerperal sepsis. He asserts that it has not lowered the mortality in these cases, and that although the temperature is usually reduced, and there is at times an improvement in the general condition, its use is not free from danger, as has been shown by Barr, Tissier, and Baldy, who claim to have seen death apparently caused by it. B. Norris has seen its use followed by erysipelas, Barr by albuminuria, and Dubrisay by dyspnoea. Spencer agrees with Olshausen that "obstetricians have derived no benefit from serum-therapy."

**Santonin.** Observing the beneficial effect of santonin in the treatment of many convulsive affections in infants and children, G. Frank Lydston<sup>2</sup> began its use in the treatment of epilepsy, and has obtained most gratifying results. He does not claim that the drug is a specific in this affection, nor to have obtained permanent cures by its use. He does claim, however, that it is quite as efficient a palliative as are the bromides, and future use may prove it to be quite as potent a curative agent. In his experience better results were obtained in the treatment of epileptic patients with santonin than with bromides. It acts well when bromides are not tolerated or fail altogether, and is free from injurious effects. In the treatment of epilepsy he employs the drug in very much larger doses than those stated in text-books, and asserts that only disappointment would follow its use if given in the doses which are ordinarily recommended. In adults the beginning dose is 2 to 5 grains (0.13 to 0.32 gm.), gradually increased to the point of tolerance. He finds that many patients tolerate doses of 20 grains given three times a day and continued for a period of some weeks. As a rule, the dose is gradually increased to about 15 grains (1 gm.) three times a day, and as the drug is not disagreeable to the taste he gives it uncombined. The action of santonin upon the genito-urinary tract is, in his experience, the best test of its tolerance. Coincidentally with an intense yellow coloration of the urine, frequent and painful micturition appears when the point of tolerance has been reached. Care should be observed in administering so powerful a drug, and the dose should be gradually increased and possible idiosyncrasies guarded against. Occasionally it becomes necessary to employ bromides as an adjuvant to the santonin treatment. Under such circumstances he suggests the use of a full dose of bromide at bedtime.

**Organic Salts and Compounds of Silver.** The investigations and results of Crédé, and also the work of Neisser, have led to the extensive

<sup>1</sup> British Medical Journal, October 14, 1899.

<sup>2</sup> Therapeutic Gazette, February 15, 1900.

use of the organic salts and compounds of silver as substitutes for silver nitrate as local antiseptics and astringents upon inflamed and infected mucous membranes, and for internal administration to replace the latter salt in many of its uses. The advantages of the most valuable of these new silver salts are that they are not precipitated by chlorides or albumin of the tissues, and therefore possess greater penetrative power than silver nitrate, and, furthermore, they are less irritating. These advantages cannot be claimed for the lactate or citrate of silver or for nargol, all of which are probably fully as irritating as silver nitrate.

ARGENTANIN, also known as ethylene diamin silver phosphate, is an antiseptic, astringent, alkaline liquid made by dissolving silver phosphate in an aqueous solution of ethyl diamin. The special claim for this preparation is that it is a powerful antiseptic, that it is not precipitated by the chlorides or albumin of the tissues, and therefore has power of deeper penetration than other antiseptics. The strength of the solution recommended in the treatment of gonorrhœa and acute infectious and chronic conjunctivitis and trachoma are from 1:5000 to 1:2000.

Kopp,<sup>1</sup> after giving it a brief trial in acute and posterior urethritis, discontinued its use, as he found it more irritating than solutions of silver nitrate. The observations of Kopp are not in accord with those of many others who consider it more penetrating and far less irritating than silver nitrate.

ARGENTOL, also known as oxy-chinolin sulphate of silver, is obtained by the action of oxy-chinolin on silver. It is an almost insoluble powder, readily decomposing in the presence of septic matter into oxy-chinolin and metallic silver, both of which in their nascent state are powerful antiseptics.

Ciprini<sup>2</sup> claims that, owing to the antiseptic value of its products of decomposition, it is superior to all other silver salts which have been decomposed from silver oxide. The salt has been employed as a dusting powder for syphilitic and other ulcers and also as an injection in oil emulsion (1:1000 to 1:3000) in acute gonorrhœa. This preparation is very slightly toxic, and has been given in daily doses of 15 grains. Being sparingly soluble in the gastric juice, it has been employed as an intestinal antiseptic. In one case of epilepsy, in one of migraine, and in one of sciatica, all depending upon auto-intoxication from intestinal decomposition, it was employed by Ciprini with asserted good results.

ARGONIN is a compound of silver and casein, and forms a white powder, which, in solution, is actively bactericidal. An opalescent, viscid, albuminous fluid, which quickly decomposes and becomes irritating, is

<sup>1</sup> Münch. med. Wochenschr., August 1, 1899.

<sup>2</sup> Allg. med. Centralbl. Zeit., August 26, 1899.

formed when argonin is dissolved in (10 per cent.) water. Solutions of this substance in water are best made by rubbing the powder with a quantity of water so as to thoroughly moisten it. Gently heat over a water-bath until the powder is dissolved, filter through glass-wool or gauze. In the strength of from 1:1000 to 7:1000 it has been used as an injection in the treatment of gonorrhœa.

Kopp<sup>1</sup> found the drug expensive, and, although less irritating, of no greater value in the treatment of gonorrhœa than silver nitrate.

A. Gutheil<sup>2</sup> was pleased with the results obtained from the use of the remedy, and noticed the disappearance of gonococci, on an average, in eight or nine days and cures in twenty-two days. On account of the tendency of solutions of argonin to decompose and become irritating, Gleason<sup>3</sup> considers it inferior to protargol in the treatment of diseases of the middle ear.

NEW ARGONIN is a light yellowish powder, slightly soluble in water, forming solutions which are quite stabile in the strength of 0.25 to 1 per cent. It has been employed as an injection in the treatment of gonorrhœa and in a somewhat weaker solution in the treatment of acute infectious and chronic conjunctivitis.

ACTOL (SILVER LACTATE) is a white, odorless, almost tasteless powder, soluble to the extent of 1:20 in water. It is decomposed by light and should be kept in dark bottles. It is a powerful antiseptic and bactericide, but is almost too irritating to be employed in the treatment of inflammations of mucous membranes.

ITROL, OR SILVER CITRATE, is a white, odorless, almost tasteless powder, soluble to the extent of about 1:4000 in water. It has been employed in the strength of 1:8000 to 1:4000 as a bactericide and astringent in the treatment of wounds. It readily decomposes when brought in contact with organic matter.

ICHTHARGON is a combination of ichthyol and silver salt, and forms a dark brown, odorless powder, soluble in water. It is recommended by L. Leistikow<sup>4</sup> in the treatment of gonorrhœa. The strength of the solution for injection should be 0.02 per cent., gradually increased to 0.2 per cent. He asserts that improvement is noted from the very beginning of the treatment.

LARGIN is a silver protalbin containing about 11 per cent. of silver. It forms a gray powder, and is soluble in about ten parts of water. The advantages of this salt over silver nitrate are that while it is actively bactericidal and astringent, it is non-irritating, and is not precipitated

<sup>1</sup> Münch. med. Wochenschr., August 1, 1899.

<sup>2</sup> Therapeutist, June 15, 1900.

<sup>3</sup> Laryngoscope, March, 1900.

<sup>4</sup> Monatsheft f. prakt. Dermatologie, August 15, 1900.

from its aqueous solution by albumin or chlorides. It may be employed for injections in acute gonorrhœa in aqueous solutions of from 0.25 to 1.5 per cent., and is also employed in the various forms of conjunctivitis in the strength of 0.25 per cent. to 0.50 per cent. In the treatment of acute gonorrhœa the best results are to be obtained by the method of Neisser.

Kornfeld succeeded in curing acute gonorrhœa in an average time of about thirty days, and rarely observed complication following its use. In posterior urethritis largin can be used in the form of Diday's irrigations ( $\frac{1}{2}$  to 1 per cent.) or Guyon's method of instillation (2 per cent.).

Stephenson,<sup>1</sup> who used largin in the treatment of a number of cases of conjunctivitis, states that even in concentrated solution it is painless, but when prolonged beyond a few weeks may stain the conjunctiva. He considers it a valuable substitute for silver nitrate in the treatment of conjunctival inflammations associated with Koch-Weeks' bacillus. In gonorrhœal ophthalmia he does not consider it as valuable as nitrate of silver or protargol.

NARGOL, OR SILVER NUCLEIDE, is a light brown powder, soluble in water, with an alkaline reaction. By long contact with chlorides it is precipitated as silver chloride, but is not precipitated by albumin.

PROTARGOL is a silver albuminose occurring as a light yellowish powder, readily soluble in water, the solutions being stabile and not precipitated by albumin, chlorides, dilute acids, or alkalies. The powder is compatible with ordinary pill excipients. Internally it has been employed in doses of from 2 to 5 grains (0.1 to 0.3 gm.) three times a day, and for instillation into the eye and for injection into the urethra 0.25 to 1 per cent. aqueous solutions have been employed. In the treatment of gonorrhœa, as soon as the diagnosis is made, Neisser orders three injections to be given three times a day, the patient being required to first urinate. Two injections were administered and retained five minutes each time, and the third injection is retained for half an hour. If the discharge is profuse the patient is required to inject every five or ten minutes for half an hour before taking a prolonged injection. After a few days, when secretion is diminished, only one prolonged injection is given once a day, and in addition an injection of bismuth and iodoform is to be taken twice a day. The strength of protargol solution at the beginning of the treatment is 0.25 per cent., and gradually increased during the progress of the case to 0.50 per cent. and then to 1 per cent. The treatment is painless, and the average length of time required to effect cures was, in Neisser's experience, about three or four weeks.

Kopp, after a very extensive use and careful study of the action of

<sup>1</sup> British Medical Journal, March 17, 1900.

protargol, states that it quickly relieves the pain of tenesmus, changes purulent discharge into a mucous discharge, lessens the number of gonococci, and in many instances leads the patient to believe himself cured, when in reality the gonococci persist and reappear in great numbers if the injections are discontinued even after having been employed for a period of some weeks. He considers the drug palliative, but in no degree more readily curative than other forms of astringent treatment. He believes that the treatment by protargol frequently gives the patient a false sense of security, when in reality his discharge remains infectious. Protargol has also been extensively employed as a substitute for silver nitrate in ophthalmic practice.<sup>1</sup> Writers agree upon its non-irritating effects, but there is still some difference of opinion as to the relative bactericidal value as compared with nitrate of silver.

Engelmann, of Bonn,<sup>2</sup> prefers 20 per cent. aqueous solutions of protargol to solutions of silver nitrate for instillation into the eyes of the new-born, and in a hundred cases in which he was sure there were infectious bacteria he observed only slight irritation following the use of protargol solution, proving it less irritating than silver nitrate. He quotes the results of Crämer upon the use of silver nitrate by the Credé method, in which in one hundred cases ninety-six were cured; more or less and sometimes enormous secretion, which usually lasted for five days or more, was frequently observed, while in 80 per cent. of the cases in which protargol was used little or no secretion was observed, and the longest duration of any secretion was a day or a day and a half. The experimental work of Hauenschild<sup>3</sup> upon the infected conjunctivæ of rabbits by instillations of from 1 to 10 per cent. solution of the drug without lessening in any degree the number of bacteria, viewed in the light of clinical results obtained by others, is rather puzzling. In the treatment of chronic suppuration of the middle ear Gleason<sup>4</sup> considers the remedy superior to all other antiseptics and astringents. His method in three cases in which he obtained most satisfaction and rapid cures was to inject a hypodermatic syringe of a 5 per cent. solution of protargol by means of a Blake canula, as high up into the attic as possible. The parts were then massaged with Siegle's pneumatic speculum in order to force a portion of the solution into the distant parts that could not be reached by the syringe, and the parts then dried with absorbent cotton. Protargol has been employed internally as a substitute for the more irritating silver nitrate in gastric carcinoma, chronic diarrhœa, and gastric and intestinal hemorrhages as a result of ulcerations, and also in the diseases of the nervous system in which silver nitrate is usually employed.

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1900, pp. 321 and 392.

<sup>2</sup> Centralblatt f. Gynäkologie, 1899, No. 30.

<sup>3</sup> Münch. med. Wochenschr., January 30, 1900.

<sup>4</sup> Laryngoscope, March, 1900.

Ruhlman<sup>1</sup> states that the daily maximum dose is 9 grains (0.55 gm.). He also states that it may be taken in larger quantities and for a longer period of time than silver nitrate before symptoms of argyria begin to appear. After prolonged use and after the patients had taken twenty-nine drachms (116 gm.) he observed slight discoloration about the mouth and on the buccal mucous membrane.

**Crede's Ointment.** This ointment has been employed with most remarkable success by a number of authors in the treatment of septic infections, such as puerperal sepsis, erysipelas, gonorrhoeal arthritis, articular rheumatism, cerebro-spinal meningitis, etc., and also in acute suppurative processes, such as phlegmon, lymphangiectasis, lymphadenitis, and furunculosis. It is made by incorporating soluble metallic silver (argentum colloidal) with an ointment base. The formula given by Cr  d   is as follows :

|                      |           |           |
|----------------------|-----------|-----------|
| R.—Argenti colloidal | . . . . . | 15 parts. |
| Aque destillat       | . . . . . | 5 parts.  |
| Cere   albe          | . . . . . | 10 parts. |
| Adipis benzoinat     | . . . . . | 70 parts. |

It is applied by rubbing into the skin, and when absorbed is said to circulate in the blood as metallic silver and to act as a most powerful bactericide. The doses usually employed are 45 grains (3 gm.) for adults and 15 grains (1 gm.) for children. But these doses have been greatly exceeded. As much as  $\frac{1}{2}$  ounce to 1 ounce (15 to 30 gm.) has been used and repeated daily for several days without giving rise to any ill effects.

**Spermin.** Spermin is a crystalline basic substance obtained from the seminal fluid of animals. It is said to exert a tonic and stimulating action upon the nervous system, and is employed in the treatment of neurasthenia or nervous exhaustion. The several salts which have been employed are spermin-auro-chloride, spermin hydrochlorate, and spermin phosphate, all of which can be given in doses of from 2 to 10 grains (0.12 to 0.60 gm.). Max Solomon<sup>2</sup> reports two cases of neurasthenia which were successfully treated by hypodermatic injections of the hydrochloride of spermin and sodium, of which 15 minims (1 c.c.) of a 2 per cent. alcoholic solution were administered hypodermatically three times a day.

**Splenic Extract.** Based upon experimental evidence that splenic extract produced hyperleucocytosis, and believing that the value of cold baths in typhoid fever is largely due to hyperleucocytosis, C. R. Carpenter<sup>3</sup> has employed splenic extract in a limited number of cases

<sup>1</sup> Therap. Beilage d. Deutsche med. Wochenschr., October 5, 1899.

<sup>2</sup> Berlin. klin. Wochenschr., August 21, 1900.

<sup>3</sup> New York Medical Record, February 17, 1900.

of enteric fever, and claims to have secured most favorable results. It is administered in doses of 5 grains (0.32 gm.) every three hours, during which time the temperature is reduced one or two degrees, after which the frequency of the dose is reduced to three times a day. The following may be found a convenient method of administering to cases with marked anæmia :

|                              |       |          |
|------------------------------|-------|----------|
| R.—Splenic extract . . . . . | 3 ij. | gm. 8.00 |
| Ferratin . . . . .           | 3j.   | gm. 4.00 |

Make into powders No. xxiv.  
One powder three times a day.

**Sodium Tellurate.** This substance is a white powder which is soluble in water and alcohol, and when given by the mouth it is eliminated by the lungs and kidneys. The only disagreeable effects of the drug which have been noted when taken in medicinal doses is a disgusting garlicky odor imparted to the breath. For the purpose of controlling night-sweats of phthisis from 2 to 5 grains (0.13 to 0.32 gm.) may be given once or twice a day. In severe cases somewhat larger doses may be employed. Barrie,<sup>1</sup> after an extensive use of the drug for the past five years, has never observed toxic effects. When unusually large doses are administered there are diarrhœa and colicky pains in the epigastrium. He employs it in doses of 4 to 5 grains (0.25 to 0.32 gm.) for four or five consecutive days. In severe cases two doses of 8 grains each may be administered. The following prescription is probably the best means of administering this substance :

|                               |             |          |
|-------------------------------|-------------|----------|
| R.—Sodii telluratis . . . . . | gr. xlviii. | gm. 3.00 |
| Extracti glycyrrhizæ, q. s.   |             |          |

Misce et ft. pil. No. xii.  
Sig.—One to two pills twice a day.

**Stypticin.** Cotarnin hydrochloride under the name of stypticin appears in the form of yellowish crystals obtained by the oxidation of narcotin. It is readily soluble in water. Stypticin is best prescribed in gelatin capsules in doses of  $\frac{1}{2}$  of a grain (0.025 gm.), of which five may be taken daily. The drug has been employed rather extensively in the treatment of menorrhagia and metrorrhagia. The advantages claimed for it over ergot and other remedies used to control uterine hemorrhage are that it is free from oxytoxic effect, and may therefore be used for controlling hemorrhage during pregnancy.

**Sulphonal.** Chronic poisoning by this substance from careless use is frequent, and in many instances comes on so insidiously as to escape detection by the physician until his attention is called to the deep port-wine color of the urine. The early symptoms, which are

<sup>1</sup> Journal des Praticiens, February 17, 1900.



frequently overlooked, are generally lassitude, weakness, nausea, and intestinal derangement, shown by slight diarrhoea or obstinate constipation. In the more advanced cases of poisoning sometimes there are griping pains in the stomach, vomiting, and paralysis, either general or confined to a limited group of muscles. Marked ataxia of the arms and legs is almost always present. The urine is of a deep port-wine color, highly acid, and later contains albumin. There is no known physiological or chemical antidote, and our course of treatment in cases of poisoning should be directed to supporting the patient and resorting to methods to assist in the elimination of the drug from the organism. Upon the earliest appearance of symptoms the drug, of course, should be discontinued, the patient given an active purge, and required to drink freely of a solution of sodium bicarbonate or mixture of magnesium carbonate (H. C. Wood<sup>1</sup>). Normal saline solutions should be administered into the colon and also given subcutaneously.

**Suprarenal Extract.** When given intravenously, water extract of the suprarenal gland produces a marked but evanescent rise of blood-pressure due to centric vasomotor stimulation and peripheral action upon the bloodvessels, and also to an increase in frequency and force of the heart's action. Howell claims that the rise of blood-pressure is due entirely to peripheral action. When an aqueous solution of the drug is applied to the mucous membrane it becomes blanched as a result of contraction of delicate bloodvessels, the effect continuing for a period of about twenty minutes to an hour. Its action upon the respiration is very slight, but when large doses are administered the respiration becomes shallow. W. H. Bates<sup>2</sup> contributes a valuable paper upon the use of suprarenal extract in diseases of the eye. In acute catarrhal conjunctivitis, in connection with other treatment, he succeeded in curing a number of cases after one or two instillations. In chronic conjunctivitis the relief afforded was only temporary; purulent cases and trachoma, although benefited, were not cured by the use of this remedy alone. In iritis it relieves congestion, but having no effect upon the constitutional symptoms it cannot bring about a cure, but materially assists atropine in producing dilatation of the pupil. Owing to its powerful astringent properties upon mucous membrane, the remedy is of the greatest value for diagnostic purposes in determining whether obstruction in the nasal duct is due to organic stricture or to swelling and inflammation of the mucous membrane. If obstruction is due to the latter cause, if syringed through the puncture into the duct it finds its way into the nose, which, of course, would be impossible in the case of organic stricture. Chronic purulent dacryocystitis usually results

<sup>1</sup> Merck's Archives, 1899, No. 11.

<sup>2</sup> Archives of Ophthalmology, 1899, xxv. 31.

from organic stricture of the nasal duct, and therefore little benefit can be derived from the use of the gland. During six years' use as an astringent Bates claims to have never seen ill effects from its use. Owing to its astringent and hæmostatic properties when combined with cocaine it is of much value in operations upon nervous persons with inflamed and congested mucous membranes. By controlling the bleeding it prolongs the anæsthetic effects of cocaine when this substance is employed in operations upon the nose or other mucous membranes.

A. G. Aldrich makes use of the following solution in operations upon mucous membranes :

|                             |         |             |
|-----------------------------|---------|-------------|
| R.—Acid. borici . . . . .   | gr. xv. | gm. 1.00.   |
| Ext. suprarenal. . . . .    | gr. xv. | gm. 1.00.   |
| Aquæ (sterilized) . . . . . | ℥ xij.  | c.c. 48.00. |
| Sig.—Mix and filter.        |         |             |

As aqueous solutions of the extract quickly decompose, solutions should be freshly made when needed, and, if so desired, may be heated to the boiling-point without injury. When used in conjunction with cocaine, anæsthesia is more perfect. It has been generally held by those who have used the gland in nasal surgery that secondary hemorrhage rarely occurs after its use, but Hopkins<sup>1</sup> asserts that after local applications of suprarenal gland these accidents are very frequent, and especially so if combined with cocaine. Probably the best preparation for local use is suprarenal extract with chloretone.

McLeod Yearsley<sup>2</sup> also used the aqueous solution (5 to 60) as a hæmostatic in rhinological operations. By applying the solution to the mucous membrane of the nose by means of cotton pledgets, as a result of its astringent effect, he was able to obtain a better view of the whole cavity, and operations were rendered almost bloodless.

Beaman Douglas<sup>3</sup> considers suprarenal extract a most important remedy in the treatment of hay fever, and speaks most enthusiastically of its action in his hands, claiming that it is almost a specific for the relief of the symptoms. He employs a watery solution of the glycerin extract for local application to the nose, and compressed tablets of the dried gland for internal use. In a later communication<sup>4</sup> he reiterates his former statements, and asserts that so constringing is the effect upon the nasal mucous membrane that if used locally and internally for a long period of time it may possibly cause atrophy. In his hands the best results have been achieved in simple cases of hay fever,

<sup>1</sup> New York Medical Journal, August 25, 1900.

<sup>2</sup> British Medical Journal, October 14, 1898.

<sup>3</sup> New York Medical Journal, September 2, 1890.

<sup>4</sup> Ibid., May 12, 1900.

where the symptoms are principally nasal and pharyngeal, accompanied by conjunctival involvement, and in cases where there are nasal lesions and the development of the disease is associated with congestion. Most satisfying results have been observed also in neurasthenic subjects having general vasomotor disturbances coupled with nasal lesions. In persons who had in former attacks developed asthmatic symptoms as a later complication the early and persistent use of suprarenal gland either decidedly modified its severity or prevented its development. If asthma has already developed the effect of the drug is not so active in controlling this complication. A few cases, however, have been seen in which, although asthmatic symptoms had fully developed, marked improvement followed the use of the remedy. In nasal cases not complicated by congestion of the nasal mucous membrane the beneficial effects are less than those with congestions. Subjects with atheromatous changes of the bloodvessels and those showing degenerative changes of the heart muscle are not improved by the use of the gland. The beneficial results from the use of the remedy should be noted within twenty-four hours by a diminution in the size of the engorged mucous membrane, relief from headache, sneezing, and coryza. Douglas does not agree with the physiological chemists who assert that when given by the mouth the drug undergoes digestion, and is thereby rendered inert. He gives 5 grains (0.30 gm.) of the saccharated dried suprarenal gland every two hours, day and night, until the patient experiences slight vertigo or cardiac palpitation, or until local examination of the nasal mucous membrane shows that the remedy is controlling the vasomotor paralysis. The periods are then lengthened to three, four, six, and finally to twelve hours, and the drug continued until the end of the attack. In conjunction with its internal use he favors local application to the nasal mucous membrane by means of a spray or upon pledgets of cotton every two hours until relief is obtained, to be repeated as required, whenever symptoms of obstruction appear. He uses a 6 to 12 per cent. solution, made by shaking the saccharated dried extract with water and macerating for an hour and decanting the clear filtrate and discarding the precipitate.

Lewis S. Somers,<sup>1</sup> after using the drug internally in twenty-one cases of hay fever, states that he has never seen good results following its use, and, furthermore, that the asthmatic symptoms were always exaggerated. He is more favorable, however, to its local application, and when used in conjunction with measures suitable to individual cases believes it to be the most satisfactory single remedy that we at present possess.

<sup>1</sup> Proceedings of the Philadelphia County Medical Society, June, 1900.

R. A. Bate<sup>1</sup> calls attention to the marked improvement in the case of Addison's disease following the use of  $\frac{1}{12}$  grain (0.005 gm.) of the extract from the suprarenal gland of sheep given three times a day. Asthenia, nausea, and pigmentation have almost disappeared after two years' treatment. Twice during this period the remedy could not be obtained for ten days, and during the interruption of the treatment the patient developed very annoying symptoms, such as severe faintness, cold sweats, muscular atrophy, and fever with bounding pulse.

Stoeltzner reports a case of rickets which showed marked improvement in nutrition during treatment with suprarenal gland. Sweating diminished, vasomotor irritability disappeared, the thorax became firmer, the teeth appeared, and the baby was able to walk at about the normal time. Spasm of the larynx was the only symptom that failed to yield to the treatment. He records a case in which an infant, while under treatment, died of bronchitis, and the post-mortem examination revealed normal calcification of the tissues and almost entire recovery from the rachitic state.

**Tannic-acid Derivatives.** On account of the tendency of tannic acid to produce gastric derangement when given for more than a few days, attempts have been made, and with considerable success, to combine it with different substances so that it may pass through the stomach unchanged and act only after entering the intestinal canal. The derivatives of tannic acid which appear to have met the requirements are tannalbin, tannigen, and tannopin, while tannoform has proven too irritating for such internal administration.

TANNALBIN is a reddish-brown powder made by the action of tannic acid upon albumin. Its dose is from 5 to 10 grains for adults and 1 to 5 grains for children. It is used in the treatment of acute, subacute, and chronic intestinal catarrh. The advantages claimed for it over the ordinary vegetable astringents are that it is entirely non-irritating, and, being insoluble in the gastric juice, it does not disturb gastric digestion. In the intestinal tract it is split up into its component parts and exerts its astringent action upon the mucous membrane. It may be given in powders, pills, cachets, or in mixtures. The following mixture will be found suitable for administering to children :

|                          |                 |      |       |
|--------------------------|-----------------|------|-------|
| R.—Tannalbin . . . . .   | 3j.             | gm.  | 4.00  |
| Sacchari . . . . .       | 3ij.            | gm.  | 8.00  |
| Acaciæ . . . . .         | 3j.             | gm.  | 4.00  |
| Aquæ cinnamomi . . . . . | q. s. ad f 3ij. | c.c. | 60.00 |

Misce. Sig.—Shake well and give a teaspoonful every two hours.

In the presence of intestinal fermentation the above mixture should, as a rule, be preceded by a laxative.

<sup>1</sup> American Practitioner and News, 1899, vol. xxviii.

TANNIGEN is a yellowish-gray, odorless and tasteless hygroscopic powder. It is insoluble in water, but freely soluble in alcohol, and is made by the action of glacial acetic acid upon tannic acid. The chemical has been employed in the treatment of diarrhoea and also as an astringent upon mucous membrane. It may be given internally to adults in doses of from 7 to 15 grains (0.50 to 1 gm.) and to children in from 2 to 5 grains (0.10 to 0.30 gm.). Charles M. Clark, reports a very severe case of diarrhoea in a tuberculous woman in whom<sup>1</sup> after failure to secure satisfactory results by the administration of other astringents, he obtained excellent results by the administration of 10-grain (0.65 gm.) doses of tannigen, combined with sodium bicarbonate, sugar of milk, and ipecac, given every two hours.

|                           |         |     |      |
|---------------------------|---------|-----|------|
| R.—Tannigen . . . . .     | 3 ij.   | gm. | 8.00 |
| Sodii bicarb. . . . .     | 3 ij.   | gm. | 8.00 |
| Sacchari lactis . . . . . | 3 j.    | gm. | 4.00 |
| Pulv. ipecac. . . . .     | gr. vj. | gm. | 0.37 |

Misce et ft. chart. No. xii.

Sig.—One powder every two hours.

On account of the hygroscopic properties of tannigen the powder should be put up in paraffin paper, or, if desired, the above prescription may be administered in cachets. The following prescription is considered valuable as a vaginal injection in the treatment of leucorrhoea :

|                                 |         |      |      |
|---------------------------------|---------|------|------|
| R.—Tannigen . . . . .           | 3 j.    | gm.  | 4.00 |
| Acidi borici . . . . .          | 3 ij.   | gm.  | 8.00 |
| Zinci sulphatis . . . . .       | gr. x.  | gm.  | 0.60 |
| Ext. hydrastis fluidi . . . . . | f 3 ij. | c.c. | 8.00 |

Misce. Sig.—Dissolve this in a cup of hot-water before adding to a three-quart syringe filled with water as hot as can be borne.

Use the injection at bedtime in a recumbent position with an obturator pipe.

For colliquative diarrhoea :

|                                 |         |     |       |
|---------------------------------|---------|-----|-------|
| R.—Tannigen . . . . .           | 3 ij.   | gm. | 8.00  |
| Bismuthi subnitratiss . . . . . | 3 iv.   | gm. | 15.00 |
| Resorcini . . . . .             | gr. vj. | gm. | 0.36  |

Misce et pone in cachetas No. xii.

Sig.—One cachet every two hours.

TANNOPIN, OR TANNON, is a chocolate-colored, tasteless, slightly odorous, hygroscopic powder which is almost entirely insoluble in water, alcohol, or ether, but dissolves in weak alkaline liquids. It is a condensation product of tannin and urotropin, containing 87 per cent. of the first and 13 per cent. of the latter. Its dose is from 7 to 15 grains (0.5 to 1 gm.), and is best administered in capsules, powders,

<sup>1</sup> Therapeutic Gazette, June 15, 1900.

tablets, or pills. It passes through the stomach unchanged, but in the intestinal tract is split up into tannin and urotropin. Its field of greatest usefulness is in the treatment of acute and chronic intestinal catarrh. In the presence of active intestinal fermentation its use should be preceded by a laxative dose of castor oil or calomel. The following prescriptions may be found useful in the treatment of diarrhœa in children :

R.—Tannopin . . . . . 3j. gm. 4.00

Fiant chart. No. xii.

Sig.—One powder every three hours.

R.—Tannopin . . . . . 3ij. gm. 8.00

Misture cretæ . . . . . q. s. f 3 iij. c.c. 90.00

Misce. Sig.—Shake well and give a teaspoonful every two or three hours.

**TANNOFORM** is a pinkish, powdery substance made by the action of tannic acid upon formaldehyde. It has been found almost too irritating for internal use, but is employed locally in the treatment of hyperidrosis and bromhidrosis. When employed locally it should be diluted with three times its weight of powdered boric acid.

**Tetanus Antitoxin.** The curative serum used in the treatment of tetanus is derived from the blood of horses rendered immune to large doses of virulent tetanus bacilli. The products to be found in the market are those of Behring, Tizzoni, and Roux, and may be procured either in the form of liquids or as a powder. E. Behring<sup>1</sup> placed upon the market a preparation which he claimed to be permanent, made so by the addition of malachite green, sodium phosphate, and toluol. In this preparation each cubic centimetre represents one unit of tetanus antitoxin, of which the initial dose is 50 to 150 antitoxin units, to be repeated in doses of from 10 to 20 c.c. at intervals of from twelve to twenty-four hours. The dry serum is twice the strength of this, and at the time of administration is to be dissolved in sterilized distilled water. With Roux and others, Behring insists that to be of the greatest value tetanus antitoxin must be given not later than thirty hours after the first onset of symptoms. The dose for children is one-half that ordinarily given to adults, and Behring considers the maximum adult single dose as 200 units. The method of Roux in standardizing the serum is to calculate how many grammes of test-animal will be protected against a four or five-day fatal dose of standard toxin. The strength is then stated to be one to so many millions. Several methods of administering antitoxin have been employed—subcutaneously, intravenously, and more recently by the intracerebral and subdural injections. Many have advised a combination of intracerebral with intravenous or subcutaneous injections. In view of the selective affinity of

<sup>1</sup> Deutsche med. Wochenschr., Leipzig, January 11, 1900.

the toxins of tetanus for the cells of a nervous tissue, Roux and Borel were led to the introduction of injections of the antitoxin into the brain, where it might be brought into direct contact with the tissues and be readily absorbed. These authors express the belief that although the inferior portion of the spinal cord should be already involved, the superior portion may yet be protected by intracerebral injections, but that the damage already done to the inferior portion of the cord cannot be repaired, and that if the superior portion of the cord is affected death will result irrespective of any methods of employing the antitoxin. They also state that in animals in which the tetanus was bulbar from the beginning, intracerebral injections will be of no more value than when given intravenously. The usual method of giving intracerebral injection is, after trephining the skull posterior to the motor area, the antitoxin is injected into the brain by means of a long needle in the direction of the lateral ventricles. Kocher's method of giving an intracerebral injection of tetanus antitoxin is as follows: The head is first shaved and thoroughly antiseptized. An imaginary line is drawn across the head from one external auditory meatus to the other. Another line is taken from the base of the nose to cross the first line at right angles on top of the head, and a third line from the outer angle of the orbit to where the first two cross each other. A point midway of the last line is the seat of operation. The skull being laid bare, a small opening is drilled with an Archimedean drill having a movable collar. The needle, which should be about two inches in length, with a round point, is attached to the syringe by about three inches of rubber tubing. It is inserted straight into the brain as far as it will go, and the injection of  $2\frac{1}{2}$  c.c. of doubly strong antitoxin is very slowly injected drop by drop. Not less than ten minutes should be consumed in making the injection of  $2\frac{1}{2}$  cubic centimetres. The wound is then closed and the injection repeated into the opposite side of the brain. Laplace<sup>1</sup> considers this a risky procedure, and expresses the belief that injections beneath the dura will meet the same indications. That intracerebral injections are not without danger and are even capable of leading to the death of the patient, as has been shown by William F. Gibbs,<sup>2</sup> who found that although the use of antitoxin by this method cured the tetanus, the boy died some weeks later as the result of the injection. In this case most careful antisepsis was practised, and Gibbs does not think that the infecting bacteria were introduced with the serum. Charles F. Cuthbert<sup>3</sup> also succeeded in markedly relieving the tetanic symptoms in a patient suffering from acute tetanus by the intracerebral injection, but this

<sup>1</sup> Philadelphia Medical Journal, March 17, 1900.

<sup>2</sup> British Medical Journal, July 1, 1899.

<sup>3</sup> Ibid., November 18, 1899.

case also unfortunately died. This method is spoken of most favorably by Semple.<sup>1</sup> James Lawrence and John Hartley<sup>2</sup> had great encouragement in the treatment of these cases by intracerebral injection. Laplace gives as a possible reason why subdural injections are preferable to subcutaneous or intravenous administration, that the bacillus, being anaërobic, the antitoxin may also be injured by aëration or oxidation, which it undergoes when given subcutaneously or intravenously, whereas when given beneath the dura it becomes absorbed and acts upon the toxins in the nerve cells without being oxidized or aërated. When used intracerebrally only small quantities of the concentrated serum should be employed. That it has been possible to save the lives of animals in whom tetanus has been induced by the use of tetanus toxin has been shown by the experiments of Knorr, Donitz, Trovel and others, but its curative value upon tetanus in men is far less convincing. In an analysis of the statistics Alexander Lambert<sup>3</sup> finds that in the reported cases by the subcutaneous and intravenous injections the death-rate in acute cases has been reduced from 88 per cent. to 72 per cent. and in chronic cases from 40 per cent. to 16 per cent. He also analyzed fifty-two cases treated by intracerebral injection. Among these nineteen recovered and thirty-three died. There were twenty-four acute cases, of which twenty-one died and three recovered, and fifteen chronic cases, of which four died and eleven recovered. Of three cases of subdural injections one chronic case recovered and two acute cases died. There are many reports of recovery from the use of antitoxin conjoined with the use of bromides, chloral, morphine, and also by the hypodermatic injection of carbolic acid, but in the greater number of these cases we believe that a careful analysis will show that the antitoxin was the least potent remedy. It should be understood that as yet the curative power of antitoxin in the treatment of tetanus in man is speculative and its best method of administration is still in the experimental stage.

**Thyroid Extract.** The value of this product in the treatment of myxœdema and cretinism is firmly established, but aside from these conditions it also has a wide field of usefulness, and reports are constantly being made upon its value in the treatment of affections some of which formerly only yielded to surgical procedures. The physiological action of the extract is but little understood, and with the intention of reconciling many of the contradictory statements as to the physiological action upon the respiration and circulation, Bela v. Fenyvessy<sup>4</sup> experimented upon rabbits with 10 per cent. solutions made by macerating in normal salt solution either the fresh thyroid of dogs

<sup>1</sup> British Medical Journal, January 7, 1899.

<sup>2</sup> Ibid., June 3, 1899.

<sup>3</sup> Medical News, July 7, 1900.

<sup>4</sup> Wiener klinische Wochenschr., February 8, 1900.



or the dry thyroid of oxen, Merck's thyroid tablets, Merck's thyroidin, and thyroid tablets from Burroughs and Welcome, of London. By the intravenous injection of any of these substances he found they lowered blood-pressure by vascular dilatation, but had little or no effect upon the heart and no constant action upon the respiration. These experiments accord with what has already been observed from its use in medicinal doses upon man, but there can be no doubt that when given in overdoses the drug is capable of inducing irregular heart action and even syncope. It is interesting in this connection to note that untoward effects of the drug, such as irregularity and overaction of the heart, may be prevented, as pointed out by Mabilie, by the simultaneous administration of moderate doses of arsenic, thereby enabling us to markedly increase the dose of the extract when it is so desired. It is probably definitely established that the active principle of the gland is iodothyrim.

The value of the preparations of the thyroid gland are not so well established in the treatment of obesity as in myxoedema and cretinism, and for that reason we welcome a number of reports in which it has been used with marked success, particularly those of Schiödtte, Sherman, and Love.

Schiödtte,<sup>1</sup> who found from his experiments upon an obese woman, in whom he carefully studied the excretions, that the loss of weight as the result of the use of thyroidin was due principally to increased destruction of the fats, but that during the early period, when a limited diet was used, the loss of weight was partially due to a destruction of body proteids. By increasing the albumin in the diet and reducing the dose of thyroidin he was able to overcome the nitrogen deficit. During eighty days the patient lost thirty pounds in weight. There was usually a slight rise of temperature during the evening and the pulse-rate was somewhat increased. Inasmuch as when given in large doses it may cause a good deal of systemic depression and even sudden collapse if used recklessly, small doses only are admissible, and the patient should be kept under observation. A. W. Sherman<sup>2</sup> reports the case of a woman, aged twenty-six years, in whom the weight was reduced from 215 pounds to 168 pounds by the thyroid treatment during a period of six months. After the fourth month the remedy was temporarily discontinued for two weeks. He thinks that by occasionally resorting to the use of thyroid in such cases weight may be kept down indefinitely. I. N. Love<sup>3</sup> has had most satisfactory results in the treatment of juvenile obesity with thyroid extract, conjoined with special

<sup>1</sup> Archiv f. Verdauungs-Krankheiten, May 6, 1899.

<sup>2</sup> Journal of the American Medical Association, March 24, 1900.

<sup>3</sup> Ibid., April 21, 1900.

attention to all hygienic rules, such as bathing and massage, and the enforcement of abundant exercises, including running, walking, jumping, horseback riding, and athletics. A boy, aged eight years, was reduced in weight from 131 pounds to 106 pounds after fourteen months' treatment. Five grains (0.30 gm.) of the extract were given three times a day, and after a time increased to four doses a day. He strongly advises that the treatment should be instituted at an early age, and that the patient should be kept under observation until maturity has been attained or until they have "outgrown" the disposition to obesity. As a means of preventing the depressing effect of the drug, and also as a general stimulant to nutrition, he employs in combination with the thyroid moderate doses of strychnine.

Hoffmeister was able to show by means of the X-ray that when the thyroid gland was removed from animals the changes in the bones were similar to those which have been observed in the bones of children suffering with myxœdema. These changes consisted in arrest of growth in the diaphyses and slow ossification of the epiphyses of the long bones. He found that when a bone was broken union was markedly retarded in many instances in animals from which the gland had been removed. From these experiments and also from a knowledge of the fact that the product of the gland is a stimulant to bone-growth, surgeons have been led to the use of thyroid in the treatment of fractures in which there was delayed union. Dr. Tronchet<sup>1</sup> reports two cases of ununited fracture in which he used thyroid extract. The first case was that of a man, aged fifty years, who had sustained a comminuted fracture of the leg, and in whom, after eighty days of treatment by the ordinary methods, and who in addition had been given calcium phosphate in large doses, massage, and even irritation, consolidation not having taken place, he was placed upon thyroid extract. Six tablets of 10 centigrammes each (1½ grains) were given daily, and after fifteen days the union was complete. The second case was one of fracture of the rib, which at the thirty-fifth day had not shown any tendency to consolidation. Thyroid treatment was instituted, and after ten days the abnormal mobility had completely disappeared. On the eleventh day of the treatment it was necessary to discontinue the use of thyroid, the patient having developed cerebral trouble. Tronchet was inclined to attribute this trouble to alcoholism instead of the use of the thyroid. Dr. Potherat, who read the report of this case before the Society of Surgery, believes that the thyroid treatment in fractures is very encouraging, but that we should not forget that the drug is capable of giving rise to untoward effects which are sometimes dangerous, and that the accident observed in the

<sup>1</sup> *Revue de Chirurgie*, January 10, 1900.

patient of Dr. Tronchet is of the nature of what we may expect in some cases from the use of this medicament.

Professor Edwin Klebs found, by removing one-half of the thyroid gland of dogs and then administering to them tuberculin, that pepsin and hydrochloric acid almost entirely disappeared from the gastric juice, and that the half of the thyroid left intact rapidly underwent atrophy, with a total disappearance of its colloidal substance. From the knowledge thus obtained from experiments, that tuberculin interfered with the thyroid function, he treated patients suffering with gastric disturbance (achylia gastrica) during the early stages of phthisis, and in whom there was atrophy of the gland, by the administration of the juice expressed from fresh thyroid glands. He reports two cases treated by this method in which the bodily condition improved and the patients gained in weight and respiratory capacity.

Mahon and Babcock look with favor upon the use of the remedy in the treatment of insanity, and particularly in cases of acute mania and melancholia with prolonged attacks, and also in puerperal and climacteric insanities, stuporous states, and primary dementia that do not respond to the usual methods of treatment. Drewry and Henderson,<sup>1</sup> after using the drug in eighty-eight cases of various forms of insanity at the Central Hospital of Virginia, are extremely skeptical as to its therapeutic value, and consider the remedy worthy of a trial only after every other rational line of treatment has been without effect.

Dr. Petrini<sup>2</sup> brought about a cure of a case of psoriasis vulgaris by the exhibition of the thyroid. Two capsules containing 10 centigrammes ( $1\frac{1}{2}$  grains) of thyroid body were given daily as a beginning dose, and gradually increased, until at the expiration of two months' time, when the patient was discharged cured, he was taking ten capsules a day. In all 543 capsules were given during the two months of treatment, and during this time no untoward effects were noted. Petrini did not observe vertigo, tachycardia, nausea, chills, or fever. The results of John E. Hays<sup>3</sup> in the treatment of three cases of psoriasis were not satisfactory, and he does not think the promise of this remedy is good in the treatment of the disease.

As an emmenagogue Glynn found the drug in doses of  $\frac{1}{2}$  of 1 grain (0.03 gm.) of extract given at bedtime to be of value in instituting the function of menstruation in temporary amenorrhœa or delayed menstruation in consequence of slight developmental changes. The dose of the dried extract of the gland is from 1 to 30 grains (0.065 to 2 gm.) daily.

<sup>1</sup> Virginia Semi-Monthly, June 22, 1900.

<sup>2</sup> Bulletin Académie de Médecine de Paris, February 20, 1900.

<sup>3</sup> American Practitioner and News, February 15, 1900.

A convenient formula for use in myxœdema, obesity, amenorrhœa, or psoriasis is as follows :

|                                |        |     |       |
|--------------------------------|--------|-----|-------|
| R.—Extracti thyroïdi . . . . . | 3 ij.  | gm. | 8.00  |
| Sodii arsenatis . . . . .      | gr. 4. | gm. | 0.016 |

Misce et ft. tabellæ compressæ No. xxiv.

Sig.—One tablet twice daily, and increase.

**Trional.** What has been said on page 404 in reference to the frequency of poisoning by sulphonal and the treatment to be resorted to in cases of poisoning is also applicable to trional poisoning. The following prescription, suggested by Pouchet,<sup>1</sup> is said to act more satisfactorily and quickly than when sulphonal is given in the form of powder :

|                                |            |      |       |
|--------------------------------|------------|------|-------|
| R.—Trional . . . . .           | gr. lxxv.  | gm.  | 5.00  |
| Olei amygdalæ express. . . . . | 3 iij.     | gm.  | 90.00 |
| Sacchari . . . . .             | 3 x.       | gm.  | 40.00 |
| Pulv. tragacanth. . . . .      | gr. xv.    | gm.  | 1.00  |
| Pulv. acaciæ . . . . .         | gr. xv.    | gm.  | 1.00  |
| Aquæ aurant. flor. . . . .     | f 3 xijss. | c.c. | 50.00 |
| Aquæ laurocerasi . . . . .     | f 3 ijss.  | c.c. | 10.00 |

Misce et ft. emul.

Sig.—Shake well and take one or two tablespoonfuls in milk at bedtime.

Each tablespoonful of the above mixture contains 7 grains of trional.

The following formula is recommended for administration by the rectum :

|                                |                     |      |        |          |       |
|--------------------------------|---------------------|------|--------|----------|-------|
| R.—Trional . . . . .           | gr. vij vel gr. xv. | gm.  | 0.50   | vel gm.  | 1.00  |
| Olei amygdalæ express. . . . . | 3 ijss vel 3 v.     | c.c. | 10.00  | vel c.c. | 20.00 |
| Vitelli, No. 1 . . . . .       |                     |      |        |          |       |
| Aquæ . . . . .                 | 3 viij.             | c.c. | 250.00 |          |       |

Warren Coleman<sup>2</sup> believes trional to be one of our safest and purest hypnotics. He has frequently administered it in doses of from 15 to 30 grains, and has never seen really dangerous symptoms follow its use. He reports the case of a woman, who during seventy-two hours took 9 drachms (36 gm.) without serious injury. When seen by him she was in a somnolent condition, from which she could be aroused. There were no respiratory or circulatory disturbances, nor was there hæmaturia. The only treatment employed was an active saline purge, and the patient quickly recovered.

**Tuberculin.** As a result of a multiplicity of tuberculins, confusion is likely to arise unless writers in their articles specify the exact product which has been employed. The term, however, always refers to either extracts or culture products of the tubercle bacillus, which is entirely different from the serum obtained from the blood of horses treated with the bacillus toxins, with which it is frequently confused. The tuber-

<sup>1</sup> Therapeutic Gazette, January 15, 1900.

<sup>2</sup> Medical News, July 28, 1900.

culins most frequently employed are the original tuberculin and the new tuberculin of Koch.

THE ORIGINAL TUBERCULIN (T. O.) is made by inoculating a culture medium of beef-broth, peptone salt, and glycerin with tubercle bacilli, and after permitting full development of the culture it is killed by heat and the liquid filtered and concentrated. The liquid thus prepared consists of the culture fluid plus the soluble products with which it is charged during the development of the culture, and also the products retained within the body of the bacilli during their growth and extracted during manufacture. It is very probable that the heat employed to kill the culture also chemically alters some of the products of bacterial growth.

THE NEW TUBERCULIN (T. R.). During the growth of the tubercle bacillus upon liquid or solid media several different substances are produced within its cell. Some of these substances are soluble and pass through the cell wall to the media upon which it is grown, while there are other products which are retained within the body of the bacillus and can only be extracted by its disintegration. The tuberculin (T. R.) is made<sup>1</sup> by cultivating virulent tubercle bacilli upon a solid medium or upon a fluid medium similar to that used in preparing the T. O. tuberculin, collecting the growth as free as possible from the culture media, disintegrating the cell by drying and grinding, and by means of glycerin and water extracting their contents. The broken and unbroken cells are removed by means of the centrifuge. Prepared in this manner it will be noted that the liquid contains only water, glycerin, and the contents of the cells.

The extensive use of the original tuberculin for diagnostic purposes by Beck in over 2000 cases, and also its use by others, is quoted by Anders,<sup>2</sup> who details its employment in his hospital and private practice. He asserts that the value of the tuberculin does not depend upon its greater reliability over the other diagnostic measures, but that it permits of a diagnosis of latent cases and also of incipient cases before the disease has sufficiently developed to be determined by other means. He deplors its less frequent use for diagnostic purposes in cases of suspected tuberculosis in which no other means are available, and particularly in incipient cases. As to the safety and accuracy of the test, he quotes an array of authorities who employed the method, and asserts that opposition comes almost entirely from those who have not employed it. In the large number of apparently healthy subjects who have shown the reaction he says that there may possibly be present in these a latent

<sup>1</sup> Deutsche med. Wochenschr., 1897, No. 14.

<sup>2</sup> New York Medical Journal, June 23, 1900.

infection. These statements are based upon sound reasoning, it having been shown that in from 30 to 40 per cent. of all the necropsies upon persons dying of other diseases there is found some unsuspected foci. He accounts for its failure to react in positive cases to a possible error in making the test—in some cases from a lack of a sufficient dose, and in others to the establishment of a tolerance brought about by multiple injections. He gives a table of 3638 cases in which tuberculin in doses ranging from  $\frac{1}{2}$  to 25 milligrammes has been employed by various authors in which the number of reactions were 2185. In another table he classifies 2014 cases into those in whom tuberculosis was suspected and in those in whom the diagnosis was undoubted. Of the former there were 1470, of which 71 per cent. reacted, and of the latter 544, of whom 78 per cent. reacted, the doses of tuberculin varying from  $\frac{1}{2}$  to 10 milligrammes. In the undoubted cases many were far advanced in the disease, and no reaction was expected. In none of the cases here recorded were there any statements made to show that tuberculin gave rise to a general infection.

T. McC. Anderson<sup>1</sup> considers tuberculin both efficacious and safe in the diagnosis and treatment of tuberculosis. Charles Dennison<sup>2</sup> considers the test highly efficacious and safe. If a reaction is not obtained in a suspicious case, as the result of too small a dose, he does not wait for several days, but nearly doubles the previous day's dose, repeated each day until the reaction is obtained. By repeating small doses at intervals of several days patients develop a tolerance, and the reaction is less likely to appear. He does not believe 10 to 12 milligrammes should be fixed as a maximum dose, and although the majority of cases tested by him began to respond to 5 milligrammes or less, he has frequently employed 15, 20, and 25 milligrammes in making a diagnosis. The determination as to whether the patient has reacted to the test is not based upon the temperature alone, but upon a feeling of general malaise, tenderness in the region of the tubercular area, and by use of the stethoscope in suspected pulmonary cases. Breath sounds become exaggerated and of a higher pitch or puerile in character if tuberculosis is present. Dr. Trudeau<sup>3</sup> has found the X-ray of value to occasionally assist him in making the diagnosis in early cases of pulmonary tuberculosis, but if additional and more conclusive evidence is required he makes use of a tuberculin test. If the initial dose of 1 milligramme is not exceeded the constitutional disturbance is slight, and no injury to the patient has in his experience ever resulted from the employment of the test.

<sup>1</sup> Lancet, June 16, 1900.

<sup>2</sup> Journal of the American Medical Association, January 6, 1900.

<sup>3</sup> Medical News, June 2, 1900.

**Urotropin** is made by the action of formaldehyde on ammonia. It forms white crystals, which are freely soluble in water. At ordinary temperatures it undergoes no change in the presence of alkalis, but in the presence of uric acid, for which the compound is a good solvent, formaldehyde is set free. When administered internally it is rapidly absorbed, probably giving up small quantities of formaldehyde to the blood. The drug is eliminated in part by the kidneys, unchanged, but is still further decomposed by the urine, with liberation of formaldehyde. The value of the drug in the treatment of diseases of the genito-urinary tract, particularly in pyelitis and ammoniacal cystitis, is dependent upon the liberation of formaldehyde, which acts as a bactericide. Nicolaier attributes its beneficial effect in the treatment of uric-acid diseases to the solvent action of formaldehyde, which is liberated upon the decomposition of the drug. The only untoward effect which has been noted when given in medicinal doses is mild vesical irritation, which is sometimes seen after its administration. Its dose is from 5 to 15 grains (0.32 to 1 gm.) in about a pint of water, given three times a day. Aside from its use in the treatment of genito-urinary diseases, urotropin is also used as a prophylactic prior to and after operations upon the genito-urinary tract, and also before catheterization. After urethrotomy the healing of the wound in some cases is retarded by contact with the urine containing decomposition products of urotropin. The following formulæ may be employed :

R.—Urotropin . . . . . 3 ij. gm. 8.00  
 Aquæ chloroformi . . . . . f ʒ viij. c.c. 250.00

Misca. Sig.—One to two tablespoonfuls in a full glass of water every four hours.

R.—Urotropin . . . . . 3 ij. gm. 8.00

Fiant chart. No. xvi.

Sig.—One to two powders in a full glass of water after meals.

**Haffkine's Prophylactic Plague Vaccine.** The prophylactic fluid of Haffkine, employed so largely and with so much apparent benefit in recent outbreaks of plague in India, consists of a liquid obtained from the bodies of the plague bacillus and their concentrated products. The method of preparing this prophylactic vaccine is as follows: A kilogramme of goat's flesh is finely chopped, macerated in a dilute solution of hydrochloric acid, and the whole heated at a pressure of three atmospheres for six hours. This is then filtered, neutralized with a solution of potassium hydrate, diluted by the addition of water up to three litres, and sterilized. This is the medium upon which the bacilli are grown. Into flasks containing this medium some fresh plague-material is placed, and in from five to fourteen days, if left undisturbed, plague bacilli, if present, will develop and form long, thread-like, stalactitic growths, hanging from the surface down into the liquid. In order to obtain a large

quantity of extracellular toxin for the prophylactic, 3-litre Pasteur flasks containing bouillon upon which is floated either cacao butter or "glee"—a kind of clarified butter—are inoculated with the culture determined to be pure and uncontaminated. The bacilli suspended from the surface of the bouillon by the "glee" grow and send down into the liquid their stalactitic growths, which are occasionally shaken off and sink to the bottom of the vessel, thereby permitting the formation of new stalactites. By this means a large quantity of the bodies of microbes is collected and the fluid is also charged with toxins secreted by the stalactites. This process is continued for five or six weeks, during which time the bodies of the bacilli undergo deterioration. The liquid is now heated in a water-bath at 65° to 70° C. for three hours, in order to kill the bacillus and render it harmless. The clear liquid is then decanted into suitable containers and is ready for use. The dose of this preparation is from 2 to 3 c.c. given subcutaneously. It is best to repeat the injection in from fourteen to twenty days, as it has been found that double inoculation more surely insures immunity than single vaccination. Although the length of time for which immunity is conferred is not definitely known, Haffkine<sup>1</sup> asserts that it confers immunity at least for one epidemic, which on the average extends from four to six months of the year. The patients after being inoculated develop moderate fever (100° to 101° F.), languor, and frequently nausea and headaches, all of which pass off in the course of about two days. Pain and sometimes swelling also is noted at the seat of inoculation. For this prophylactic Haffkine claims that it not only confers immunity from disease in a very large majority of cases upon whom it is used, but in those who are so unfortunate as to contract the plague it pursues a milder course, and the case mortality is markedly reduced. That these claims have been abundantly verified may be seen from the numerous reports of tens of thousands of persons vaccinated during the recent epidemics of plague in India. The inoculations are harmless, having been given in the extremes of age—a child of ten days and a woman of ninety years have received the injections without experiencing any ill effects. Patients suffering with plague, and also those who are incubating the disease, should not be vaccinated, as it has been shown that if given at this time it does not cut short nor limit the severity of the attack, but rather magnifies the severity—in addition to the usual symptoms of plague we have those of the reaction of the prophylactic.

In addition to the prophylactic of Haffkine there have been used in the treatment of plague the curative serum of Yersin and also that of Lustig. The curative serum of Yersin<sup>2</sup> is made by injecting into the

<sup>1</sup> British Med. Journ., July 1, 1899.

<sup>2</sup> Annales de Institut Pasteur, 1897, xi. p. 81.



veins of horses recent cultures of the plague bacillus (forced cultures upon gelatin) until the animals are immunized. Three weeks after the last injection the horse is bled and serum collected. Yersin reports in this paper twenty-three cases of plague, treated as follows: Six patients, who were in the first day of the disease, all recovered without the supuration of the bubo in from twelve to twenty-four hours; 20 to 30 c.c. of the serum were employed. Six cases were in the second day of the disease; all recovered in from three to four days without suppuration of the bubo, 30 to 50 c.c. of serum being used. Four cases were in the third day of the disease, and all recovered, 40 to 60 c.c. of serum being used. Three cases were in the fourth day of the disease, all of whom recovered in from five to six days; in only one case was there a supuration of the bubo; 20 to 50 c.c. of serum were used. Four cases were in the fifth day of the disease; of these, two died, 60 to 90 c.c. of the serum being used. Unfortunately, these results have not been verified by a general use of the serum, and evidence was given before the Plague Commission<sup>1</sup> that the first curative serum that was tried was that of Yersin, and all agreed that it was negative.

LUSTIG'S CURATIVE SERUM is made by immunizing horses by injections of the toxins of plague bacilli and collecting the serum from the blood of these animals. The reports of Golotti<sup>2</sup> speak favorably of the serum. The value of these curative sera is still to be determined by future use.

**Wright's Prophylactic Vaccine against Typhoid.** Wright's prophylactic against typhoid consists of a fluid containing the dead typhoid bacteria and the specific toxins which have been elaborated by these bacteria in the course of their cultivation on 1 per cent. peptone bouillon. Briefly outlined, the process of manufacture consists in inoculating peptone bouillon contained in a cultivation flask with virulent cultures of typhoid bacilli. After being inoculated with the micro-organisms, these flasks containing bouillon are incubated at blood-heat for a period of from fourteen to twenty days. At the expiration of this time, by the application of heat in a water-bath at a temperature of 60° C., the bacteria are killed. The next step consists in standardizing the prophylactic and adding to it as a preservative one-tenth of its bulk of a 5 per cent. solution of lysol or carbolic acid. The dose of Wright's<sup>3</sup> vaccine varies from 8 to 25 minims (0.5 c.c. to 1.5 c.c.), according to its strength as tested by its opacity and also by its toxic power upon guinea-pigs. The most reliable statistics as to the immunizing properties of this vaccine are to be gathered from the reports of its use upon the English

<sup>1</sup> British Medical Journal, April 29, 1899, p. 1043.

<sup>2</sup> Ibid.

<sup>3</sup> Ibid., January 20, 1900.

troops in India and South Africa. From December, 1898, to November, 1899, more than 11,000 troops were under observation, and of these 8460 were non-inoculated and 2835 inoculated. Of the non-inoculated 213 contracted typhoid fever, and of these 23 died; of the inoculated 27 contracted the disease, and of these 5 died. It should be remarked that none of the troops included in these statistics had ever before suffered from enteric fever. Among the inoculated cases the majority were young men, who, it is well known, are more liable to the disease than those of more mature age. Furthermore, the greater number of those inoculated were unseasoned troops, who had only recently been sent to India and as yet were unacclimated. On the other hand, the non-inoculated, as a rule, were older men, and by longer residence in India had become acclimated.

These results are favorable to the use of antityphoid inoculations, especially so, considering the unfavorable circumstances under which they were made.

The prophylactic vaccine should not be confused with antityphoid serum, which has been used to a limited extent as a curative agent in the treatment of enteric fever.

# INDEX.

- A** BORTIVE treatment of gonorrhœa, 70  
Abscess, periostitis and extra-articular, 214  
Absorption, 284  
Achyilia gastrica simulating hyperchlorhydria, 34  
Acoïn, 323  
Actinomycosis, 74  
treatment of, 74  
Actol, 400  
Airol, 324  
Albuminuria, 223  
Albumosuria, 227  
Alcohol, coffee tea, cola, and maté, significance of, for the function of the muscles, 283  
influence of, in the secretion of milk, 284  
supposed albumin-saving action of, 284  
Alkaptonuria, 231  
Amœbic dysentery, 51  
treatment of, 52  
Amylene hydrate, 324  
Anæsthesia, 115  
examination of the blood with reference to, 100  
of the spinal cord, 347  
Anæsthetic, selection of, in surgery, 115  
later effects of, 117  
Ankylostomiasis, 53  
Antipneumococcus serum, 325  
Antistreptococcus serum, 396  
Antitetanus serum, 127  
methods of injection, 127  
varieties of, 127  
Antitoxin, diphtheria, 359  
tetanus, 410  
Antitubercle serum, 326  
Antivenomous serum, 327  
Apomorphine, 329  
Appendicitis, 50  
treatment of, 50  
Argentanin, 399  
Argenti nitras and its compounds, 398  
Argentol, 399  
Argonin, 399  
new, 400  
Arsenauro in diabetes mellitus, 66  
Arsenic, 330  
Arthritis, acute, in which the effusion or exudate is sterile, 172  
contains bacteria, 172  
or synovitis, 170  
Arthritis, acute, or synovitis, not associated with injury, 171  
pathology of, 171  
gonorrhœal, 174  
of the hip, 182  
primary and secondary, 172  
traumatic, 164  
pathology of acute, 165  
pyogenic infections in acute, 164  
treatment of acute, 166  
Arthropathies associated with nervous lesions, 187  
in syringomyelia, 188  
Asperin, 335  
Assimilation, faulty, a cause of phthisis, 45  
Auditory centres of the cerebral cortex, 298  
Auto-intoxication, 197  
as the cause of pancreatic diabetes, 286  
of the gastro-intestinal tract, 45  
treatment of, 45
- B** LADDER, 81  
bleeding from, 83  
tumors of, 81  
typhoid infection of, 82  
ulcer of, 81  
Blood, 287  
examination of, in surgical cases, 98  
in traumatic shock, 98  
with reference to general anæsthesia and operative procedures, 100  
serum, reaction of the animal organism toward foreign, 282  
Bones, surgery of, 162  
tuberculosis of, 202-207  
situation of, 207  
Bottini's operation, 85  
Brain, circulation and œdema of, 289  
Bread and butter, 26  
Bright's disease, skin eruptions occurring in, 234  
relation of, to syphilis, 255  
treatment of, 247  
Bromides, 334  
Bromipin, 334  
Bromoform, 336
- C** ACODYLATE of sodium, 331  
Calcium eosolate, 338  
Calculi, 76  
in the ureter, 76  
Carbolic acid, 339

- Carbon monoxide, amount of, in tobacco smoke, 293  
 Carbonic acid gas, 342  
 Castor oil, 343  
 Castration, 85  
 Cerebral cortex, auditory centres of, 298  
   vessels, innervation of, 289  
 Chancre, digital, 87  
 Charcot's joint, 187  
 Chest, cause of collapse or death from blows upon lower, 93  
 Chloretone, 344  
 Circulation, 287  
   and oedema of the brain, 289  
   of the blood in the area of paralyzed nerves, 290  
 Cocaine, 346  
   subarachnoid injection of, 347  
 Cocainization of large nerve trunks to prevent shock, 91  
 Colon, dilatation of, 50  
 Color blindness artificially produced, 299  
 Constipation, 48  
 Coronary arteries of the heart, circulation of, 289  
 Coxa vara, 144  
   traumatica adolescentium, 151  
   infantum, 144  
   treatment of, 159  
 Credé's ointment, 403  
 Creosotal, 353  
 Creosote, 352  
   carbonate, 353  
   phosphate, 353  
   valerianate, 353  
 Cresoform, 353  
 Crurin, 357  
 Cystinuria, 232  
 Cystitis, treatment of, 83
- DIABETES** mellitus, arsenauero for, 66  
   milk diet for, 66  
   pancreatic, auto-intoxication as the cause for, 286  
 Diarrhoea, summer and hot weather, 45  
   treatment of, 46  
 Digestion, 284  
 Digestive tract and allied organs, diseases of, 17  
 Digitalis, 357  
 Dionin, 375  
 Diphtheria antitoxin, 359  
 Disease, spreading of, 310  
   transference of, by insects, 316  
   by rats, 316  
 Diseases, avoidance, restriction, and prevention of, 321  
   not known to be specific, yet due to toxins, 304  
   of the kidneys, 223  
   principal modes by which the ordinary communicable, are contracted, 317  
   by ingestion, 317  
   by inhalation, 317
- Diseases, principal modes by which the ordinary communicable, are contracted by way of the eyes, 317  
   are spread, 314  
   specific, 309  
   the causation of, 303  
 Disinfection, 321  
 Dislocation of the elbow-joint, 140  
 Diuretics, 273  
 Dormiol, 360  
 Duodenal ulcer, perforating, 49  
 Duotol, 354  
 Dust, infectious, 314  
 Dysentery, amoebic, 51
- EAR**, the labyrinth of, 300  
   Elbow-joint, dislocation of, 140  
   fracture at the, 135  
 Electrolysis, stricture of the œsophagus and, 18  
 Emphysematous cellulitis, 122  
   differential diagnosis between, and malignant oedema, 122  
   gangrene, 122  
   prognosis of, 124  
 Epicarin, 360  
 Epigastrium, causes of collapse or death from blows upon, 93  
 Epilepsy, 307  
 Epiphyseal separation at the lower end of humerus, 135  
   of the epicondyles, 137  
   of the lower apophysis of the humerus, with dislocation, 140  
 Epiphysis at the lower end of the humerus, 135  
 Epiphyses, partial separation of all four, 140  
 Erythema uræmicum, 237  
 Erythrol tetranitrate, 361  
 Eumenol, 362  
 Euphthalmin, 362  
 Eyes, contraction of diseases by way of, 317
- FAT**, amount of, in the glands during state of hunger, 283  
 Femur, curvature of the neck of, 144  
   differential diagnosis in conditions about the hip-joint and upper end of, 158  
   excision of the head of, in old fractures of the femoral neck, 162  
   fracture of the neck of, in infants, 150  
 Fertilization and the artificial production of normal larvæ from the unfertilized eggs of the sea-urchin, 277  
 Fibrinogen, origin of, 287  
 Fluorine, 363  
 Formaldehyde, 363  
 Fortoin, 366  
 Fracture at the elbow-joint, 135  
   of neck of the femur in adults, 165  
   in infants, 150  
   treatment of, 159

- Fractures, dislocations, amputation, surgery of the extremities and orthopedics, 91  
of the femoral neck, excision of the head of the femur in, 162
- GALL-BLADDER, 57**  
Gallstones, 66  
Röntgen ray for detection of, 66
- Gangrene, emphysematous, 122  
multiple spontaneous, in association with acute infections, 133  
in malarial fever, 130
- Gas bacillus, 122  
conclusions as to the, 125
- Gastric douche, 21  
secretion and indicanuria, relation between, 43  
ulcer, 28
- Gastro-intestinal disease, otitis media and the causation of, 319
- Gelatin, 103, 366  
hæmostatic effect of, 79  
use of, 103  
in aneurism, 107  
internal use of, 104  
local use of, 103  
solution for internal use, 104
- Geosol, 355
- Glands, 293
- Gonococcus, cultivation of, 178  
infection, 67  
treatment of, 68  
local, 69
- Gonorrhœa, 197  
abortive treatment of, 70  
chronic, and gleet, 69  
dilators in, 70  
treatment of, 69
- Gonorrhœal arthritis, 174  
of the hip, 182  
treatment of, 70
- Guaiacol, 352  
carbonate, 354  
phosphite, 356  
valerianate, 355
- Guaiacophosphal, 356
- Guaiamar, 356
- Guaiasanol, 355
- HÆMATURIA, essential renal, 78**  
treatment of, 79
- Haffkine's prophylactic plague vaccine, 419
- Heart, secondary rhythms of the normal human, 288
- Hedonal, 369
- Heredity, facts and laws of, 279
- Hermann von Helmholtz, brain of, 296
- Heroin, 377
- Hetol, 369
- Hip, tuberculosis of, 218  
conservative orthopedic treatment of, 218
- Hip-joint and upper end of femur, differential diagnosis in conditions about, 158
- Holocain, 369
- Hot air of high degree, 370
- Humerus, epiphyseal separation at the lower end of, 135  
of the lower apophysis with dislocation of, 140  
epiphyses at the lower end of, 135  
the X-ray shadow of the lower end of, 136
- Hydrogen peroxide, 372
- Hydrops articolorum intermittens, 196  
classification, 196  
idiopathic, 198  
relation to other arthropathies, 199  
symptomatic, 196  
auto-intoxication, 197  
chronic arthritis, 197  
gonorrhœa, 197  
infection, 197  
osteomyelitis, 196  
tuberculosis and lues, 197  
uric-acid diathesis, 197  
treatment of, 200
- hypostrophos, 195  
tendo-vaginarum, 199
- tuberculosis, 205
- Hygiene, 303
- Hyperchlorhydria and hypersecretion, 25
- ICHTHALBIN, 372**  
Ichthargon, 400
- Incubation, period of, 320
- Indicanuria, 43
- Infections, 122  
gas bacillus, 122
- Infectious diseases are distributed from the throat, 318  
dust, 314  
spray, 315
- Infusion, choice of solution, 112  
conditions in which it should be practised, 113  
intraperitoneal, 109  
per rectum, 110  
salt water, 107  
subcutaneous method, 111
- Ingestion, contraction of disease by, 317
- Inhalation, contraction of disease by, 317
- Inoculation, 316
- Insects, transference of disease by, 316
- Intestinal absorption of saline cathartics, 286  
contents, chemical reaction of, 285
- Intestine, 45  
motor influence of splanchnic nerve on, 48
- Intraperitoneal infusion, 109
- Iodine, occurrence of, in the thyroid and thymus glands, 294
- Ion-proteid compounds and their rôle in the mechanics of life, 278
- Ions, effect of, upon myogenic and neurogenic rhythmical contractions, 279  
upon embryonic and muscular tissue, 279

Isochymia caused by pyloric stenosis, 33  
sweet oil in treatment of, 33  
Irol, 400

**JOINT**, change and destruction of, 172  
contusion or distortion of, 166  
study of a simple contused, 169  
tuberculosis of, and results of, 216  
wounds of, 170

Joints, remote effects of contusion or distortion, 169  
surgery of, 162  
tuberculosis of, 202

Justus' test, 87

## KIDNEY, 77

Kidneys, diseases of, 223  
internal secretion of, 259  
mode of action of certain poisons, 242  
tuberculosis of, 72

## LARGIN, 400

Larynx, physiology of, 301  
Leucocyte count as an aid to differential diagnosis in various surgical conditions, 102

Leucocytosis following hemorrhage, 99

Leukæmia, 66

Lipoma aborescens tuberculorum, 206

Lipomasia, 215

Lithiasis, glycerin as a remedy for, 77

Liver, 57

floating, 57

clinical significance of, 65  
definition of, 58  
diagnosis of, 61  
differential diagnosis of, 64  
etiology of, 58  
symptomatology of, 60  
treatment of, 64

Lumbar puncture, 119

for diagnostic purposes, 119  
therapeutic purposes of, 121

Lungs, exchange of gases in, 292

Lymphatics, 53

## MALARIA, multiple gangrene in, 130

Malarial fever, 311

mosquito in, 311

what has reduced, 313

Malignant edema, 122

Malpighian bodies, development of, 257

Mammary gland, 374

Melancholia, condition of stomach in, 44

Menthol valerianate, 383

Metabolism, 280

experiments with proteids containing phosphorus and those free from it, 281

influence of food on, 280

sexual function and, 281

Methylene-blue, 383

Micro-organisms, pathogenic, 320

Middle ear in cold and warm weather, 318

Milk of nursing women, 76

pasteurization of, 25

Morphine derivatives, 375

physiological action of, on respiration, 292

Mosquitoes, classification of, 312

Motor centres in cerebral cortex of man, 297

Mould in stomach and its probable significance, 38

treatment of, 43

## NARGOL, 401

Nephritis, treatment of, 247

unilateral, surgical treatment of, 77

Nervanin, 385

Nerve ending in a voluntary muscle, 296

regeneration and degeneration of motor and sensory, 296

fibres, functional adaptability of apparent, 296

medullated, arising in the spinal ganglia of mammals, 295

Nervous system, 295

Neurasthenia, 304

## EDEMA, acute circumscribed, relation of idiopathic joint effusion to, 199

Œsophagus, 17

diverticulum of, 17

spasm and atony of, 18

stricture of, 18

Optic projection of the retinal meridians, 300

Orphol, 386

Orthoform, 386

Osteomyelitis, 196

further progress of the bone focus in, 212

gross appearance of, 210

tubercular, 209

Otitis media and the causation of gastrointestinal disease, 319

Ovarian extract, 388

Oxycamphor, 388

Oxyphor, 388

## PALLADIUM chloride, 389

Pancreas, 54

Pancreatic diabetes, auto-intoxication as the cause of, 286

digestion, 54

juice, influence of bile acids and alkalies on, 284

Pancreatitis, 55

diagnosis of, 56

symptomatology of, 55

treatment of, 56

Paralyzed nerves, circulation of blood in area of, 290

Parotid gland, 389

Pasteurization of milk, 25

Pericarditis in renal disease, 239

- Periostitis and extra-articular abscess, 214  
 Petroleum, 389  
 Petrosulfol, 390  
 Phosphorus, 390  
 Phosphotal, 353  
 Phthisis, faulty assimilation a cause of, 45  
 Physiological heart poisons, 290  
 Physiology, 277  
     general, 277  
 Picric acid, 393  
 Pilocarpin, 393  
 Pituitary body, physiological effects of, 293  
 Plague, prevention of, 322  
     vaccine, Haffkine's prophylactic, 419  
 Poisons, mode of action on kidney, 242  
 Potassium chlorate, 394  
 Prevention of disease, 321  
 Prostate, 84  
     malignant tumors of, 84  
     senile enlargement of, 84  
 Protargol, 401  
 Prototherapy, 391  
 Protozoan parasites, cycle in man and mos-  
     quitoes, 311  
 Pupil, width of, 298  
 Pus infections, 75  
 Pyloric stenosis, hypertrophic, in infancy,  
     32  
     sweet oil in the treatment of ischo-  
     chymia caused by, 33
- R**AYNAUD'S disease, 130  
     Receptaculum chyli, obliteration of, 53  
 Renal disease, pericarditis in, 239  
     tumors, 250  
 Resaldol, 394  
 Respiration, 287  
     physiological action of morphine on,  
     292  
 Respiratory gas exchange, 291  
 Retinal meridians, optic projections of, 300  
     veins, cause of the physiological pulsa-  
     tion of, 299  
 Rheumatism, acute joint, 185  
 Rheumatismus articularis acutus, 185  
 Röntgen rays for detection of gallstones, 66
- S**ALINE cathartics and intestinal absorp-  
     tion, 286  
 Salol, 395  
 Salt-water infusion, 107  
     methods of, 107  
     therapeutic use of, 107  
 Sanarelli's serum, 395  
 Santonin, 398  
 Scarlet fever, 309  
 Serum, antipneumococcus, 325  
     antistreptococcus, 366  
     antitetanus, 127  
     antitubercle, 326  
     antivenomous, 327  
     Sanarelli's, 395  
 Sexual function and metabolism, 281  
 Shock, literature on, 97  
     surgical, 91
- Silver citrate, 400  
     lactate, 400  
     nucleide, 401  
     organic salts and compounds of, 398  
 Skin eruptions occurring in Bright's disease,  
     234  
 Sodium tellurate, 404  
 Solanin, poisoning by potatoes containing,  
     25  
 Special senses, 297  
     and orientation, 300  
 Specific diseases, 309  
 Spermin, 403  
 Spina ventosa, 208  
 Spinal cord, anesthesia of, 347  
 Splanchnic nerve, motor influence on the  
     intestines, 48  
 Splenic extract, 403  
 Spray, infectious, 315  
 Spreading of disease, 310  
 Stapedius muscle, function of, 300  
 Stomach, 19  
     acute dilatation of, 29  
     atonic dilatation of, 31  
     cancer of, 29  
         blood in, 29  
     conditions of, in melancholia, 44  
     erosions of, 27  
     methods of diagnosis, 19  
     mould in, 38  
     powder blower, 22  
         indications for, 24  
         method of using, 23  
     shape and position of, 27  
     syphilis of, 35  
 Strychnine in treatment of shock, 99  
 Stypticin, 404  
 Subarachnoid injections of cocaine, 347  
 Subcutaneous infusion, 111  
 Sulpho-guaiaacolate of potassium, 355  
 Sulphonal, 404  
 Suprarenal extract, 405  
     effect of, in smooth muscles, 294  
 Surgery of the bones and joints, 162  
 Synovial membrane, tuberculosis of, 202  
 Synovitis not associated with injury, 171  
     or acute arthritis, 170  
     pre-tubercular or irritative, 203  
     tubercular, 204  
 Syphilis, 86  
     and marriage, 87  
     late hereditary, 88  
     of the stomach, 35  
     relation of, to Bright's disease, 255  
     treatment of, 88  
     visceral, 89  
     without primary sore, 87  
 Syringomyelia, arthropathies in, 188
- T**ANNALBIN, 408  
     Tannic-acid derivatives, 408  
 Tannigen, 409  
 Tannon, 409  
 Tannopin, 409  
 Test-meals, 20  
 Tetanus antitoxin, 410

- Tetanus, present treatment of, 177  
 preventive vaccination of, 128  
   conclusions, 129  
   subcutaneous and intravenous serum  
   treatment of, 126
- Therapeutic referendum, 323
- Thiocol, 355
- Throat, infectious diseases distributed from,  
 318
- Thyroid and thymus glands, 294  
   extract, 412  
   gland, chemistry and physiology of,  
   294
- Tobacco smoke, amount of carbon monoxide in, 293
- Toxins, 303
- Treatment of actinomycosis, 74  
   of acute arthritis, when exudate or effusion is sterile, 172  
     when it contains bacteria, 172  
   of amoebic dysentery, 32  
   of appendicitis, 50  
   of atonic dilatation of stomach, 31  
   of auto-intoxication from the gastrointestinal tract, 45  
   of Bright's disease, 247  
   of constipation, 48  
   of curvature of neck of femur, 159  
     in adults, 160  
   of cystitis, 83  
   of gonococcus infection, 68  
   of gonorrhœa, chronic, 69  
   of gonorrhœal arthritis, 70  
   of hæmaturia, 79  
   of hydrops articulorum intermittens, 200  
   of late hereditary syphilis, 88  
   of mould in the stomach, 43  
   of pancreatitis, 56  
   of shock, 97  
   of stomach, 19  
   of summer diarrhœa, 46  
   of tetanus, 126  
   of traumatic arthritis, 166  
   of tuberculosis of bones and joints, 217  
     of the hip, 219  
   of unilateral nephritis, 77
- Trional, 416
- Tubercle bacilli in the urine, 73
- Tubercular involvement of the bone and cartilage, 213  
   joint, changes in, 215  
   osteomyelitis, 209  
     further progress of the bone focus, 212  
     gross appearance of, 210
- Tubercular synovitis, 204
- Tuberculin, 416  
   new, 417  
   original, 417  
   reaction of, 217
- Tuberculosis, 71  
   and lues, 197  
   end results of bone and joint, 216  
   hydrops, 205  
   of bones and joints, 202  
     diagnosis of, 217  
     treatment of, 217  
   of the diaphysis of the short bones, 208  
   of the hip, 218  
     conservative treatment of, 218  
     early exploratory operation, 221  
     iodoform injections, 219  
     modern treatment of, 220  
     orthopedic treatment of, 219  
     plaster of Paris dressing, 219  
   of the kidney, 72  
   of the synovial membranes, 202  
   raw meat in treatment of, 72
- Tumors, renal, 250
- Typhoid vaccine, Bright's prophylactic, 421
- U**LCER, duodenal, perforating, 49  
   gastric, 28
- Uræmia, nature of, 259
- Ureter, calculi in, 26  
   operation on, 80
- Uric acid, 262, 268, 282, 283  
   diathesis, 197
- Urine, tubercle bacilli in, 73
- Urotropin, 419
- Utricle, 85
- V**ASCULAR system, physiology and mechanism of, 290
- Vasectomy, 85
- Venous pulse, 290
- W**ORD DEAFNESS, a case of, 298  
   Wright's prophylactic vaccine against typhoid fever, 421
- X**-RAY shadow of the lower end of the humerus, 136
- Y**ELLOW fever, 310









FEB 21 1902

JUL 22 1902

JUN 10 1903

